VOL. 2, NO. 3, 2023
ISSN 2772-963X

RESEARCH LETTER

# Ultrafast Power Doppler for Detecting Intraoperative Myocardial Perfusion in Infants With Critical Congenital Heart Disease

Abnormal myocardial perfusion is a cause of reoperation and long-term morbidity in transposition of the great arteries (TGA) and hypoplastic left heart syndrome (HLHS). Intraoperative clinical studies found that patients who had evidence of abnormalities in the coronary microvasculature have an increased association with adverse events. The current reference technique for assessing adequate coronary blood flow is by quantifying the velocity of moving blood volume through the myocardium. Assessing temporal changes of blood volumes within the epicardial coronary arteries throughout the cardiac cycle is a complementary technique that can be useful in elucidating etiologies of myocardial dysfunction including distal coronary obstruction and issues in autoregulation of the microvasculature. However, direct assessment of temporal changes of blood volumes in the coronary microvasculature has been challenging due to technical limitations on spatiotemporal resolution of current clinical imaging modalities.[1] The recent development of ultrafast ultrasound imaging (UUI) with power Doppler techniques has enabled the quantification of blood volumes within the coronary microvasculature down to the level of the coronary pre-arterioles (~100 μm).[2,3] This imaging technique was validated against gold standard coronary flow probe assessment in an animal model.[4] The temporal resolution of UUI enables direct quantification of blood volume changes of the coronary microvasculature throughout the cardiac cycle.[1] As UUI devices are portable, they can be deployed in the operating room allowing immediate assessment of coronary microperfusion before and after procedures involving the coronary vessels.

The objective of this study was to evaluate whether ultrafast power Doppler (UPD) detects temporal changes in myocardial blood volumes in bypass surgery for critical congenital cardiac disease. We hypothesized that UPD could detect changes in intraoperative perfusion patterns in neonatal TGA and HLHS.

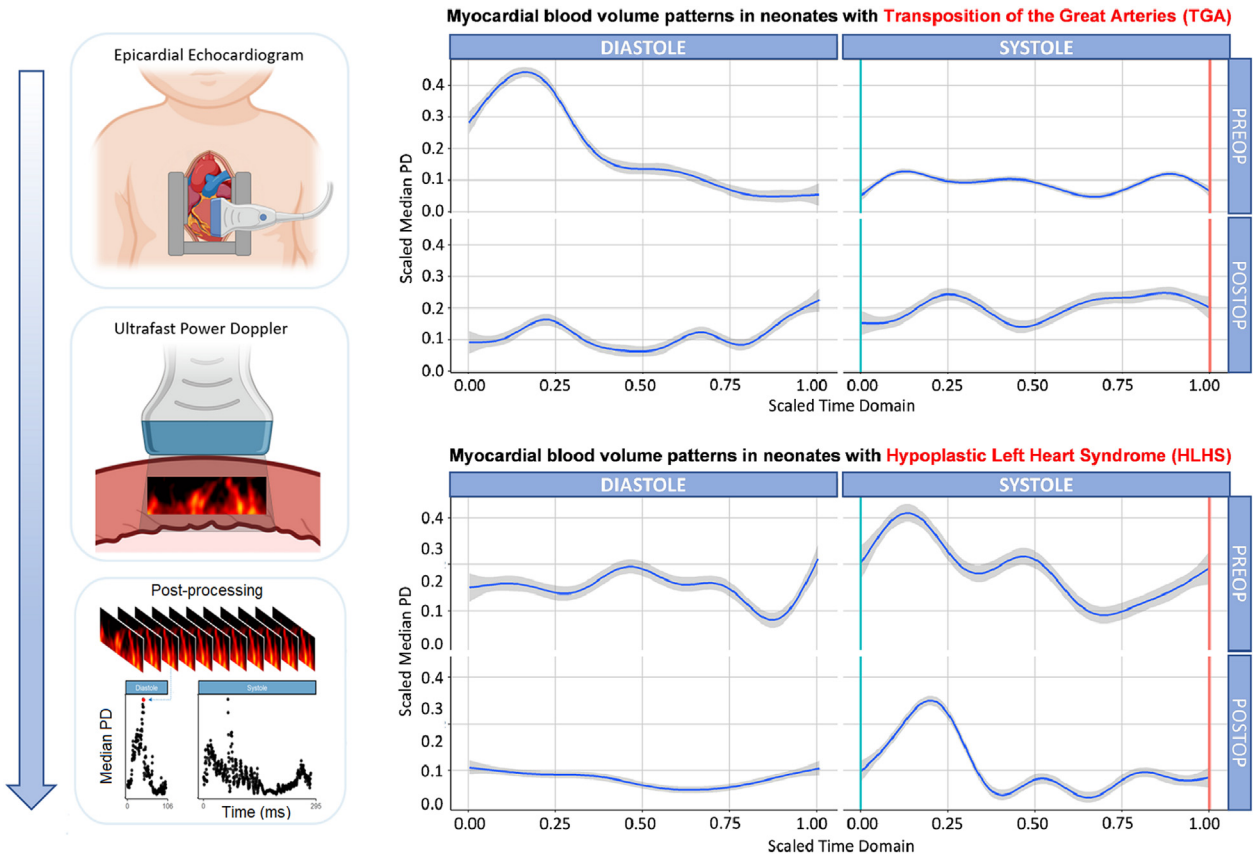
UPD was performed on each patient using a programmable ultrafast ultrasound system (Vantage 256, Verasonics Inc) with a linear array probe (11L, 6.9 MHz, GE Healthcare). The UPD acquisition methodology has been described in previous works by our team.[5] Epicardial echocardiography was performed in the operating room by the surgeon who positioned the probe using conventional focused B-mode imaging. Right ventricular epicardial UPD acquisitions were obtained immediately before/after cardiopulmonary bypass in TGA undergoing the arterial switch operation (ASO) or HLHS undergoing stage 1 Norwood/Sano palliation. We visualized temporal UPD patterns by plotting the median PD of each frame over time (see **Figure 1**, left panel). We integrated the changes in UPD signals (Power Integral [PI]) in systole and diastole to compare blood volume shifts. Two-way repeated measures ANOVA (analysis of variance) compared cardiac cycle and operative status to PI. The study was approved by the local review ethics board (REB number: 1000070089), and all parents gave written informed consent.

We included 5 TGA and 5 HLHS. Other than their diagnosis, there was no significant difference between the 2 groups in terms of demographics (including age, sex, and weight). Bypass and cooling times were similar across the TGA and HLHS groups.

In children with TGA, the preoperative UPD temporal pattern was notable for a peak in early diastole which then falls to a lower value and levels off in systole. The postoperative UPD pattern is notable for a lack of the distinctive early diastolic peak seen preoperatively (**Figure 1**, right panel). Meanwhile the HLHS group maximum values were in early systole and the visual temporal patterns did not change significantly from preoperative to postoperative acquisitions (**Figure 1**, right panel).

For the TGA group, ANOVA testing revealed no significant difference in PI values when comparing preoperative to postoperative PI values ($P = 0.384$) or

**FIGURE 1** Myocardial Perfusion Pattern Acquisition and Visualization by Ultrafast Ultrasound




**(Left)** Ultrafast ultrasound epicardial acquisitions are taken in the operating room in neonates with congenital heart disease. The right ventricular myocardium is scanned using dedicated ultrafast sequences and power Doppler (PD) signals are processed. The median PD of the region of interest is obtained on a frame-by-frame basis. In this figure, the values of a single patient with transposition of the great arteries' preoperative right ventricular free wall acquisition is displayed. **(Right)** Results before and after surgery for transposition of the great arteries and hypoplastic left heart syndrome. The median power Doppler (PD) of each frame in the acquisition was plotted as a function of time. PD was scaled to the peak median PD value obtained in that acquisition's entire cardiac cycle. Time was scaled to the length of that phase's duration. **Blue vertical line** denotes mitral valve closure and **orange vertical line** denotes mitral valve opening. This figure was made, in part, with Biorender.com. HLHS = hypoplastic left heart syndrome; TGA = transposition of the great arteries.

diastolic to systolic PI ($P = 0.152$) in isolation. However, there was a statistically significant interaction between operative status (ie, pre- or post-ASO) and cardiac cycle on PI ($P = 0.021$), suggesting that cardiac cycle's effect on myocardial blood volumes is affected by change in coronary circulation (before/after ASO) in TGA patients. Pairwise comparisons revealed that there was a 25% decrease in PI in systole relative to diastole in TGA patients preoperatively though it is not statistically significant (mean difference = −17, percent difference = −25%; $P = 0.11$), but postoperatively there was a significant increase in blood volumes in systole compared to diastole (mean difference = 66.6, percent difference = 140%; $P = 0.027$). For the HLHS group there was a significant difference in PI while comparing cardiac cycle in isolation ($P = 0.044$), but no significant difference while looking at operative status by itself ($P = 0.115$) or in combination with cardiac cycle ($P = 0.389$). In other words, there is a difference in blood volumes in systole compared to diastole, but this relationship does not change after the Norwood operation is performed. On pairwise comparisons there was an increase in PI in systole compared to diastole preoperatively (mean difference = 72.4, percentage difference = 140%;

$P = 0.00079$), yet this increase was maintained postoperatively (mean difference = 23, percentage difference = 176%; $P = 0.0043$).

This study demonstrates that UPD can detect intraoperative temporal changes in myocardial blood volumes in infants undergoing bypass surgery. Our approach directly builds on the work by Maresca et al[4] who first validated the use of ultrafast ultrasound myocardial perfusion assessment in a swine model. In their study, they specifically assessed UUI techniques to approximate coronary flow reserve compared to an epicardial flow probe. In contrast, we focused on temporal changes in blood volumes and additionally assessed UPD's clinical feasibility to approximate myocardial perfusion in the operating room.[5] We did this in 2 ways: 1) by studying its temporal pattern throughout the cardiac cycle; and 2) by quantifying the relative difference in blood volumes in systole and diastole. We found that the temporal patterns in myocardial blood volumes in the TGA right ventricle changed after ASO while the temporal patterns in the HLHS right ventricle were unchanged before and after Norwood Sano. Future studies should validate the absolute quantification of blood volumes and apply this technique in other clinical settings. Discovering ways this tool could be complementary to current myocardial perfusion imaging techniques would be an important next step.

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https://doi.org/10.1016/j.jacadv.2023.100290



This study was supported by Canadian Institutes of Health Research (CIHR), 202203PJT- 183888; Canada Foundation for Innovation (CFI) and the Ministry of Research and Innovation, Canada; Natural Sciences and Engineering Research Council of Canada (NSREC), Canada (RGPIN-2021-03539); Thrasher Research Fund (#15473); and the Labatt Family Heart Center at the Hospital for Sick Children, Toronto, Canada. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.
Meryl Cohen, MD, MS Ed, served as the Associate Editor for this paper. Michael Landzberg, MD, served as the Guest Editor-in-Chief for this paper.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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