Haemodynamic inefficiencies during stress hold key for comprehensive assessment after Fontan operation

Joao F. Fernandes, PhD, Hannah Bellsham-Revell, PhD, MD, James Wong, PhD, MD, Caner Salih, PhD, MD, Kuberan Pushparajah, PhD, MD, Pablo Lamata, PhD, Adelaide de Vecchi, PhD

PII: S2666-2507(23)00409-1
DOI: https://doi.org/10.1016/j.xjtc.2023.11.003
Reference: XJTC 1558

To appear in: JTCVS Techniques

Received Date: 18 October 2023
Revised Date: 24 October 2023
Accepted Date: 25 October 2023


This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Copyright © 2023 The Authors. Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery
Haemodynamic inefficiencies during stress hold key for comprehensive assessment after Fontan operation

Joao F. Fernandes, PhD¹; Hannah Bellsham-Revell, PhD, MD²; James Wong, PhD, MD²; Caner Salih, PhD, MD²; Kuberan Pushparajah, PhD, MD¹,²; Pablo Lamata PhD¹; Adelaíde de Vecchi, PhD¹

¹School of Biomedical Engineering and Imaging Sciences, King’s College London, 5th Floor Becket House, Lambeth Palace Road, London SE1 7EU, UK
²Department of Congenital Heart Disease, Evelina London Children’s Hospital, Guy’s & St Thomas’ Hospital, London, SE1 7EH, UK

Disclosure Statement
No author has any conflict of interest relevant to this study.

Funding Statement
Authors received funding support from AMR grant GN2977; the Wellcome/EPSRC Centre for Medical Engineering [WT203148/Z/16/Z]. Furthermore, the authors acknowledge support from the Department of Health and Social Care (DHSC) through the National Institute for Health and Care Research (NIHR) MedTech Co-operative award for Cardiovascular Diseases to Guy’s & St Thomas’ NHS Foundation Trust in partnership with King’s College London.

Word Count: 826 words.

Corresponding Author Contact Information
Joao Filipe Fernandes
School of Biomedical Engineering & Imaging Sciences 5th Floor Becket House, 1 Lambeth Palace Road, London SE1 7EU

King’s College of London
Central Picture. Flow analysis at rest and stress based on catheterisation and MRI data.

Central Message
Post-Fontan operation arterial stiffness and flow haemodynamics are altered in stress leading to preload restriction, 73% afterload increase and severe restrictive retrograde flow towards myocardial perfusion.

Main Text
In hypoplastic left heart syndrome (HLHS) and variants, the Damus-Kaye-Stansel anastomosis (DKS) affects the shape of the reconstructed aorta, and subsequently its conduit function and the myocardial workload. The DKS also provides vital retrograde flow towards the coronaries (1-2). We present a case of critical aortic stenosis with a borderline left ventricle (LV), where 4D Flow analysis revealed new mechanistic insights into the relationship between DKS remodelling and flow.

Case history
A 5.5-year-old boy with a systemic RV, a hypertrophied LV, endocardial fibroelastosis, and a dilated DKS underwent comprehensive post-Fontan operation follow-up for symptoms of effort intolerance following institutional ethical approval (21/LO/0650, 9/28/2021) (Fig.1). Informed consent for publication of study data was provided.

He had initially undergone balloon aortic valvuloplasty to resolve critical aortic stenosis followed by the hybrid procedure (bilateral pulmonary artery banding and ductal stent
insertion). At post-hybrid imaging, the LV contributed 25% of the cardiac output. Biventricular repair was however rejected due to restrictive LV physiology and the risk of the left heart becoming unable to support the systemic circulation without the development of pulmonary hypertension. Therefore, the patient underwent arch reconstruction and DKS with hemi-Fontan operation at 1 year 4 months. An incision was made along the underside of the transverse arch and down the ascending aorta to the level of the transected main pulmonary artery. The distal arch and descending aorta were sutured together along their adjacent margins using continuous 6-0 Prolene. An incision was made down the medial aspect of the descending aorta and a patch of donor pulmonary homograft was used to augment the arch. A V-shaped cut in the main pulmonary artery was made adjacent to the native ascending aorta and the two vessels were sutured together. The patient then proceeded to fenestrated lateral tunnel Fontan completion at 3 years 8 months.

Cardiac Magnetic Resonance Imaging acquisition, including 4D Flow, and simultaneous cardiac catheterisation were performed post-Fontan operation during rest (FiO₂ 0.3) and pharmacological stress (FiO₂ 0.3, Dobutamine 10mcg/kg/min) under general anaesthesia. The systemic RV showed adequate contractile reserve (end-systolic volume: 27 ml/m² at rest vs 17 ml/m² at stress) and inotropic response (end-systolic elastance $E_{ES}$: 1.22 vs 1.59), Fig.1B. Diastolic function improved during stress with the isovolumetric relaxation constant decreasing from 62ms to 18ms. Despite this, preload fell (mean end-diastolic wall stress: $89 \times 10^3$ dynes/cm² vs $70 \times 10^3$ dynes/cm²), suggesting limited pulmonary venous return (3). Ventricular afterload simultaneously increased (arterial elastance $E_A$: 1.52 vs 2.63), signalling a deterioration of coupling between neo-aorta and systemic RV ($E_A/E_{ES}$: 1.25 vs 1.65).

To characterise this afterload non-invasively, aortic pressure gradients and energy inefficiencies were quantified from 4D Flow MRI data (4). The highest increases in systolic pressure gradients under stress occurred in the DKS (3.1 mmHg) and descending aorta (7
Pulse wave velocity analysis showed a significant stiffness increase at the proximal descending aorta (61.1 Kpa at rest vs 163.6 Kpa at stress). At peak systole, vortical flow in the DKS caused a 2.5-fold raise in energy dissipation during stress (Fig.1C). These inefficiencies cumulatively increased the afterload by 73%, as measured by $E_A$. In systole, the native aortic flow fed the upper aortic branches, while the neo-aortic flow was mostly channelled into the descending aorta (Central Picture A-B). In diastole, retrograde flow from the descending aorta perfused the upper branches before entering the native aorta with minimal vortical motion at rest (Fig.2A). In contrast, during stress, it formed spiralling vortices with low velocity and delivered 53.8% less mean flow rate to the coronaries (Fig.2B-C). Antegrade flow was also present in the neo-aorta in early diastole in both conditions (Central Figure C-D).

**Discussion**

This case showed that the increase in afterload during stress caused aorto-ventricular uncoupling despite an adequate RV response. This functional burden was due to stiffness changes and flow inefficiencies, which potentially reinforced LV hypertrophy and DKS dilation (5-7).

Interestingly, different aortic segments have adapted to perform complementary functions in systole and diastole. While the native aorta fed the upper branches during systole, the descending aorta supported upper body perfusion in diastole. The diastolic flow to the coronaries was disrupted during stress, due partly to momentum dissipation in the dilated DKS, partly to the fact that, despite the RV’s ability to relax, the aorta was unable to do so. This could be caused by the stiffer vascular tone recorded at stress without a significant increase in end-systolic pressure. This approach shows the value of 4D Flow MRI to assess proxy metrics for identifying ventriculo-arterial decoupling without the need for catheterisation. Furthermore,
the analysis of the stress datasets provides the first evidence of the sensitivity of coronary flow
to the DKS remodelling, which is not apparent during rest. Although it is known that RV-
dominant patients with hypertrophied LV commonly exhibit lower hyperaemic myocardial
blood flow (8), no data exist on the role of the DKS remodelling in myocardial perfusion. Stress
4D Flow MRI could thus be used to identify patients at risk of subclinical subendocardial
ischaemia despite good RV function and no anatomical obstruction, improving patient
selection for treatment before myocardial damage occurs.
References


Supplemental References


Figures

Fig 1  A: 3D MRI angiography of the DKS anastomosis. B: Pressure-Volume loops of the systemic right ventricle at rest and under pharmacological stress. C: 4D Flow MRI streamlines showing the vortex in DKS region at peak systole. D: Comparison of conduit function at rest and stress, assessed by the advective pressure drop along the aortic length at peak systole [3].

Fig. 2 A-B: 4D Flow MRI streamlines of retrograde flow from the descending aorta into the native aorta at rest and stress, respectively. C: Diastolic retrograde flow: consistently with the flow dynamics shown in panels A and B, the retrograde flow rate is higher at rest than at stress, with dashed lines indicating mean flow rates (6.1 ml/s vs 3 ml/s).