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Loïc Georges Macé, Marien Lenoir. Rethinking the pathophysiology of Fontan circulation: insights from Kenji Sunagawa and Arthur Guyton. *Interdisciplinary Cardiovascular and Thoracic Surgery*, 2025, 40 (3), <10.1093/icvts/ivaf056>. <hal-05469625>

HAL Id: hal-05469625

<https://hal.science/hal-05469625v1>

Submitted on 21 Jan 2026

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Cite this article as: Macé LG, Lenoir M. Rethinking the pathophysiology of Fontan circulation: insights from Kenji Sunagawa and Arthur Guyton. *Interdiscip CardioVasc Thorac Surg* 2025; doi:10.1093/icvts/ivaf056.

Rethinking the pathophysiology of Fontan circulation: insights from Kenji Sunagawa and Arthur Guyton

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Received 7 January 2025; accepted 2 March 2025

Keywords: Fontan operation • ventriculo-arterial coupling • ventricular-vascular coupling • venous return • univentricular heart • physiology

Dear Editor,

The recent article by Joeri Van Puyvelde *et al.* [1] presents two key dichotomous observations in patients with a Total CavoPulmonary Connection (TCPC):

1. 'Patients with right ventricular dominance experienced progressive decline due to systolic dysfunction'.
2. 'Patients with left ventricular dominance exhibited failure due to diastolic dysfunction [graphical abstract]/restrictive pathophysiology [abstract] or high pulmonary vascular resistance'.

The authors rightly point out that 'The specific pathophysiological pathways leading to failure in TCPC patients are not yet fully understood' and that 'Understanding these mechanisms is crucial for guiding treatment strategies, facilitating personalized management and developing preventive measures' [1].

In our view, these crucial challenges could be anticipated and met by revisiting two fundamental principles of cardiovascular physiology described more than half a century ago:

1. Ventriculo-arterial coupling, described by Kenji Sunagawa *et al.* [2], underpins the intrinsic predisposition of the Fontan circulation to a 'contractility-afterload mismatch by means of increased impedance caused by additional connection of the pulmonary vascular bed to the systemic vasculature' [3]. This mismatch particularly compromises the systemic right ventricle, whether it functions in a biventricular circulation or, more critically, as the single dominant ventricle in the Fontan circulation. This has been previously demonstrated by Andrew Redington [4], who noted: 'Both patient groups (post-Mustard and post-Fontan patients) show evidence of abnormal ventricular-vascular coupling'.
2. Venous Return, as conceptualized by Arthur C. Guyton, highlights the profound impact of resistance to venous return. Guyton's demonstration that 'A small increase in venous resistance decreases cardiac output eight times as much as an increase in arterial resistance of similar magnitude' [5] is highly

relevant in the Fontan circulation, where pulmonary vascular resistance—equal to venous resistance [6]—is the main determinant of venous return. This principle explains the diastolic dysfunction observed after the completion of the Fontan circulation, described as 'restrictive pathophysiology' by Joeri Van Puyvelde *et al.* [1].

Unlike the first principle, where systolic dysfunction results from a contractility-afterload mismatch and mainly affects a dominant right ventricle, the chronic increase in venous return resistance—equal to pulmonary vascular resistance—leads to sustained unloading of the single ventricle, whatever its dominant morphology. This raises a crucial question: could systolic dysfunction mask diastolic dysfunction (as defined in the study) in cases of right ventricular dominance? If so, this would explain why diastolic dysfunction is more evident in cases of left ventricular dominance.

Furthermore, the association observed between high pulmonary vascular resistance and left ventricular dominance, as noted by Van Puyvelde *et al.* [1], does not appear to be supported by robust data in their current study. Further exploration is therefore required to support or refine this conclusion.

ACKNOWLEDGEMENTS

Artificial intelligence (ChatGPT, OpenAI, 2024) was used to correct language, grammar and spelling, while preserving the author's intended message.

FUNDING

The authors received no funds for the conduct of this study.

Conflict of interest: none declared.

DATA AVAILABILITY

There are no data in this letter.

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