Commentary: Dream big in every small step

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The last stage of surgical single-ventricle palliation has undergone ingenious modifications since its first description.\(^1\) The achievement of a higher arterial saturation level by the separation of the venous backflow from the systemic circulation at the cost of a passive, nonpulsatile pulmonary blood supply and higher systemic venous pressure has led to the initially successful but challenging Fontan physiology in the longer follow-up.\(^2,3\) By consideration of various etiologies for an ultimately failing Fontan circulation, the search for the optimal fourth stage palliation strategy continues, with remarkable future potential.\(^4\) A progressively increasing pulmonary vascular resistance is one of the critical factors that may hinder an effective pulmonary blood flow and thus lead to the failure of the Fontan circuit. Our focus seems to shift from observing the rough global hemodynamic parameters to the changes in anatomic properties and endothelial function of the pulmonary microvasculature. A remodeling of the pulmonary vasculature and its endothelial dysfunction with an altered reactivity to vasoactive agents may ensue as a result of a chronic nonpulsatile pulmonary flow with low shear stress.\(^5\)

In this issue of the *Journal*, Latus and colleagues\(^5\) report the invasive assessment of pulmonary endothelial function in a limited number of patients with a Fontan circulation. As this is the first report of its kind, Latus and colleagues\(^5\) are to be congratulated for their innovative approach in an important effort to improve the understanding of pulmonary endothelial function in patients with a Fontan circulation. In this novel approach, invasive left lower lobe pulmonary artery Doppler and pressure measurements enabled the local assessment of the pulmonary vascular resistance and pulmonary flow reserve in response to acetylcholine. Latus and colleagues\(^5\) report a drop in local pulmonary vascular resistance after injection of acetylcholine in a posterior branch of the lower lobe pulmonary artery with a diameter of 3 to 5 mm. An interesting observation was that in patients in New York Heart Association functional class III, a blunted response to acetylcholine with a paradoxical increase in local pulmonary vascular resistance was observed, which significantly differed from patients in New York Heart Association functional class II, who had a decrease in local pulmonary vascular resistance. A significant relationship was found between baseline local pulmonary vascular resistance and the pulmonary flow reserve, whereas the local hemodynamics did not correlate with such global measurements as the pulmonary arterial pressures or global pulmonary vascular resistance. The time after establishment of Fontan circulation did not have an effect on local hemodynamic properties.

The methods that Latus and colleagues\(^5\) have utilized had previously been successfully used for other indications.\(^6-9\) The low sample size, the missing cardiac magnetic resonance imaging in some patients, and the solely local assessment of endothelial function in an attempt to understand its global impact on the pulmonary vascular resistance hinder liberal conclusions that can be made from the results in this study. The understanding of the microvascular properties with the use of pharmacologic aids indeed has the potential to guide future primary and secondary preventive strategies to alleviate long-term deleterious effects of low–shear stress circulation on the pulmonary vasculature. This study is therefore of importance in leading these efforts, particularly in patients with a Fontan circulation. The feasibility of the methods has already been shown in this study; however, further research is warranted to prove the prognostic value of the local endothelial function and its translation to the clinical setting in this subset of patients.

We thank Latus and colleagues\(^5\) for their excellent contribution.
References