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Experimental investigation of the effect of non-Newtonian behavior of blood flow in the Fontan circulation

Andrew L. Cheng [a,*], Niema M. Pahlevan [b,c], Derek G. Rinderknecht [d], John C. Wood [a], Morteza Gharib [d,e]

[a] Division of Pediatric Cardiology, Department of Pediatrics, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA
[b] Department of Aerospace and Mechanical Engineering, University of Southern California, Los Angeles, CA, USA
[c] Huntington Medical Research Institutes, Pasadena, CA, USA
[d] Graduate Aerospace Laboratories, California Institute of Technology, Pasadena, CA, USA
[e] Department of Medical Engineering, California Institute of Technology, Pasadena, CA, USA

HIGHLIGHTS

- A Newtonian fluid assumption is typically used in cardiovascular simulations.
- Non-Newtonian behavior has significant influence in regions of low-shear flow.
- We evaluated non-Newtonian behavior in a model of the low-shear Fontan circulation.
- Non-Newtonian behavior affected flow patterns and shear stress distribution.
- The Newtonian fluid consistently underestimated power loss vs. non-Newtonian fluid.

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ABSTRACT

The Fontan procedure for univentricular heart defects creates a unique circulation where all pulmonary blood flow is passively supplied directly from systemic veins. Computational simulations, aimed at optimizing the surgery, have assumed blood to be a Newtonian fluid without evaluating the potential error introduced by this assumption. We compared flow behavior between a non-Newtonian blood analog (0.04% xanthan gum) and a control Newtonian fluid (45% glycerol) in a simplified model of the Fontan circulation. Particle image velocimetry was used to examine flow behavior at two different cardiac outputs and two caval blood flow distributions. Pressure and flow rates were measured at each inlet and outlet. Velocity, shear strain, and shear stress maps were derived from velocity data. Power loss was calculated from pressure, flow, and velocity data. Power loss was increased in all test conditions with xanthan gum vs. glycerol (mean $10 \pm 2.9\%$ vs. $5.6 \pm 1.3\%$, $p = 0.032$). Pulmonary blood flow distribution differed in all conditions, more so at low cardiac output. Caval blood flow mixing patterns and shear stress were also qualitatively different between the solutions in all conditions. We conclude that assuming blood to be a Newtonian fluid introduces considerable error into simulations of the Fontan circulation, where low-shear flow predominates.

1. Introduction

Blood is a complex two-phase fluid of formed elements (such as red blood cells and platelets) suspended in plasma, an aqueous solution of proteins, salts, and organic molecules [1]. While blood is a non-Newtonian fluid with shear-thinning behavior (i.e. its apparent viscosity decreases as shear rate is increased) [1], its flow characteristics have been observed to approximate Newtonian fluid behavior in large arteries [2]. As such, the assumption of blood as a Newtonian fluid is common in computational and in vitro experimental studies of cardiovascular biofluid mechanics. In general, the non-Newtonian properties of blood are only apparent at shear rates less than 100 s^{-1} [3]. However, non-Newtonian behavior has been shown to have a significant influence in the microvasculature [4] and in a variety of settings where low-shear flow is more prevalent [5–7]. In particular, non-Newtonian behavior can

* Correspondence to: 4650 Sunset Blvd., Mailstop #34, Los Angeles, CA 90027, USA.
E-mail address: acheng@chla.usc.edu (A.L. Cheng).

Abbreviations: XG, xanthan gum; SVC, superior vena cava; IVC, inferior vena cava; RPA, right pulmonary artery; LPA, left pulmonary artery

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affect velocity profile blunting, flow separation, energy dissipation, and magnitude and distribution of wall shear stress [4,8,9]. Multiple blood rheology models have been utilized in numerical and computational simulations including Casson, Carreau–Yasuda, K–L, power law, and Lattice Boltzmann models to better incorporate these non-Newtonian flow characteristics [10].

In the cardiovascular system, wall shear stress plays an important role in maintaining normal blood vessel function and growth [2]. Normal levels of arterial wall shear stress (10–70 dyne/cm^2) promote endothelial quiescence and expression of atheroprotective mediators, while abnormally low wall shear stress (<4 dyne/cm^2) leads to endothelial proliferation and production of atherogenic substances [11]. Generally, the normal wall shear stress range in arteries is an order of magnitude larger than that in veins [11]. However, in patients who have undergone the Fontan procedure, the final stage of surgical palliation for univentricular congenital heart defects, blood from the central systemic veins (superior vena cava [SVC] and inferior vena cava [IVC]) bypasses the heart and directly flows into the pulmonary arteries [12]. Therefore, by its very design the Fontan procedure exposes the pulmonary arterial bed to abnormally low wall shear stress. This chronic non-pulsatile pulmonary blood flow has been shown to lead to endothelial dysfunction in these patients by altering the responsiveness of endothelial nitric oxide synthase [13,14].

Although the Fontan procedure has significantly improved early survival, these patients are still at risk for early mortality as well as severe long-term dysfunction of the heart, lungs, liver, and intestines [15,16]. Therefore, significant research efforts have been made to try to optimize the surgery in order to minimize these complications. In large part due to experimental models demonstrating the energetic efficiency of various Fontan configurations, the Fontan procedure has evolved over the last three decades to the current extracardiac conduit and lateral tunnel techniques [17]. While technological advances have allowed for the development of more sophisticated models over time, for simplification computational models have universally assumed blood to be a Newtonian fluid [18–21] and experimental models have used Newtonian fluids [22–24] without any evaluation of the potential error introduced by this assumption. Extrapolating from prior investigations of non-Newtonian behavior in blood vessels [4,5,7–9], treating blood as a Newtonian fluid could result in incorrect conclusions about power loss, pulmonary blood flow distribution, and distribution of wall shear stress. Despite this, a few centers have started to use computational fluid dynamics with a Newtonian assumption to design an optimal Fontan conduit for clinical use [19,25]. Although the performance metrics predicted by computational models were promising, the clinical success of these Fontan conduits unfortunately has been limited so far [19,26].

The goal of this investigation was to evaluate how a Newtonian fluid assumption affects flow in an experimental model of the Fontan circulation. We hypothesized that in comparison to a Newtonian fluid, a non-Newtonian fluid would demonstrate different flow profiles, decreased hydraulic efficiency, decreased mixing of inlet flow streams, and larger areas of low wall shear stress.

2. Methods

2.1. Fluids

A solution of xanthan gum in water (XG) was used as the experimental non-Newtonian fluid. Dynamic viscosity was measured using a DV2T cone/plate viscometer (Brookfield AMETEK Inc., Middleborough, MA) at 37 °C at 12 shear rates in the range of 1–1000 s^{-1}. A concentration of 0.04% by weight was determined to have similar viscosity to a typical Fontan patient [27]. For interpolation of viscosity between data points for shear rates of 0–30 s^{-1}, viscosity was determined by a Herschel–Bulkley fluid model [28]:

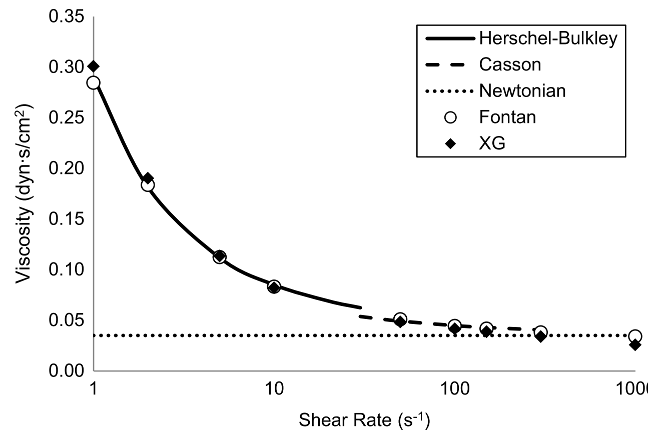

Fig. 1. Viscosity measurements of 0.04% xanthan gum solution closely matched published viscosity data of Fontan patients. For interpolation between data points, viscosity was estimated with a Herschel–Bulkley model for shear rates of 0–30 s^{-1}, a Casson model for 30–300 s^{-1}, and as a constant Newtonian viscosity for 300–1000 s^{-1}.

$$\mu = k\dot{\gamma}^{n-1} + \frac{\tau_0}{\dot{\gamma}} \tag{1}$$

where τ_0 is the yield stress, $\dot{\gamma}$ is the shear strain, and k and n are constants with $k = 8.9721$ cP s^{-1}, $n = 0.8601$, and $\tau_0 = 20$ mPa. For shear rates of 30–300 s^{-1}, viscosity was determined by a Casson fluid model [28]:

$$\mu = \left[\sqrt{\tau_0\left(\frac{1-e^{-m\dot{\gamma}}}{\dot{\gamma}}\right)} + \sqrt{\mu_\infty}\right]^2 \tag{2}$$

where μ_∞ is the Newtonian viscosity, m is a constant, and other variables are defined as above with $\tau_0 = 0.06$ dyne/cm^2, $\mu_\infty = 0.035$ dyne/cm, and $m = 100$ s. For shear rates greater than 300 s^{-1}, viscosity was modeled as Newtonian at 3.5 cP [28]. The viscosity curve of the XG solution is illustrated in Fig. 1. The density of the XG solution was 913.3 kg/m^3.

A solution of 45% glycerol in water by volume was used as a control Newtonian fluid with viscosity of 3.5 cP. The density of the glycerol solution was 1099.3 kg/m^3. For the PIV measurements, both fluids were seeded with 10–45 μm fluorescent polyethylene microspheres with 532 nm excitation and 605 nm emission peaks (Cospheric LLC, Santa Barbara, CA).

2.2. Fontan circuit model

A model of the vena cavae and pulmonary arteries was custom-made from glass. Model dimensions were based on prior similar in vitro studies [22,29]. Fig. 2 shows a schematic of the mock Fontan circuit. The glass model was submerged in either XG or glycerol, depending on the experimental condition, and connected to the rest of the circuit with rigid tubing. Resistance in each limb was controlled with adjustable external clamps. Steady flow was supplied from the reservoir into the circuit using a S-MOT100 centrifugal pump (Orqis Medical, Lake Forest, CA) controlled with a Levitronix LUI flow controller (Levitronix GmbH, Zurich, Switzerland).

The glass model was illuminated using a Gemini PIV 200 Nd:Yag laser (New Wave Research, Fremont, CA) pulsed at 14 Hz. Time intervals for the particle exposures ranged from 450 μs and 5 ms.