Fluid structure interaction model analysis of cerebrospinal fluid circulation in patients with continuous-flow left ventricular assist devices

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ABSTRACT

Purpose: The current 1-dimensional fluid structure interaction model (FSI) for understanding cerebrospinal fluid (CSF) circulation requires pulsatility as a precondition and has not been applied to patients with continuous-flow left ventricular assist devices (CF-LVAD) where pulsatility is chronically reduced. Our study aims to characterize the behavior of CSF pressure and flow in patients with CF-LVADs using a computational FSI model.

Methods: Utilizing the computational FSI model, CSF production in choroid plexuses of the 4 ventricles was specified as a boundary condition for the model. The other source of production from capillary ultrafiltrate spaces was accounted for by the mass conservation equation. The primary CSF absorption sites (i.e., arachnoid granulations) were treated as the outlet boundary conditions. We established a low pulse wave to represent patients with a CF-LVAD.

Results: From the model, low pulse conditions resulted in a reduction in CSF pressure amplitude and velocity though the overall flow rate was unchanged.

Conclusions: The existing FSI model is not a suitable representation of CSF flow in CF-LVAD patients. More studies are needed to elucidate the role of pulsatility in CSF flow and the compensatory changes in CSF production and absorption that occur in patients with CF-LVADs in whom pulsatility is diminished.

Keywords: Cerebrospinal fluid circulation, Computational modeling, Fluid structure interaction model, Left ventricular assist devices

Introduction

The cerebrospinal fluid (CSF) system is strongly coupled with the cardiovascular system and is key to understanding the pathophysiology of cerebrovascular and craniospinal disease (1). Two components have been postulated to affect the CSF circulation: 1. bulk flow and 2. pulsatile flow (2). In the bulk flow component, CSF flow is driven by a hydrostatic pressure gradient between the site of formation at the choroid plexus and site of absorption at the arachnoid granulations. In the pulsatile flow component, CSF flow is driven by the phase difference in cerebral blood inflow and outflow resulting in pulsatile movement of CSF throughout the cranial and spinal subarachnoid space (1).

A coupled hydrodynamic model of the cardiovascular and CSF system using a transfer function based on in vivo phase-contrast MRI measurements of CSF flow and cerebral blood flow was proposed by Martin et al (1). This coupled model has been used to study CSF flow where pulsatile flow has been thought to be essential to normal brain function (3). Disturbances in the natural CSF flow pattern are associated with diseases such as hydrocephalus, syringomyelia, or Chiari malformation (3-5). The current model describing CSF flow is based on Reymond’s equation that requires pulsatility as a

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Cerebrospinal fluid circulation in patients with CF-LVADs

Fig. 1 - (A) Schematic computational diagram of the complete circle of Willis. (B) Schematic representation of the cerebrospinal fluid (CSF) circulation with boundaries (i.e., arachnoid granulations) depicted in red. (C) Representative transcranial Doppler ultrasound waveform and M-mode readings of blood flow in the Circle of Willis for a patient with a continuous-flow left ventricular assist device.

precondition (6). CSF flow has not been studied in conditions where the pulse is diminished.

This is the case for patients with implantable continuous flow left ventricular assist device (CF-LVAD) technology. CF-LVADs have gained widespread use as an effective therapy for patients with advanced congestive heart failure (7). Unlike normal physiologic pulsatile blood flow from the native heart with cyclic ventricular ejection, CF-LVADs continuously unload the heart with smaller variation in end-diastolic and end-systolic volume, leading to diminished pulsatility and near continuous blood flow (8). Given the unique blood flow physics of this patient population, it provides the opportunity to assess the advantages and limitations of the simplified cylindrical FSI model as a representation of CSF flow.

Therefore, our study aims to characterize the behavior of CSF pressure and flow in patients with CF-LVADs with a presumed low arterial pulse using a computational fluid structure interaction (FSI) model.

Materials and methods

In this study, we utilized the principles of Reymond’s 1-dimensional model to simulate arterial segments within the brain and spinal cord and couple the cardiovascular system with the cerebrospinal fluid system using computational fluid dynamics (Fig. 1A). We constructed the CFS motion and fluid dynamic simulation for our FSI model to account for the curvature, variable cross sections of the CSF flow path and friction using the same approach as described by Gupta et al (6). Following this, we modeled the pulse wave propagations for our model using the equations and calculations depicted below in Equation [1], and incorporated the boundary condition values based on their MRI studies.

\[
\begin{align*}
\dot{A} + (\dot{u}A) &= \psi \\
\dot{u} + \left( \frac{u^2}{2} + \frac{\nu}{2} \right) &= \frac{\nu}{2} u'' - \frac{K}{2} u - K_{\text{head}} u^2 \text{sign}(u) + \frac{\nu}{2}
\end{align*}
\]

Here: \(A\) is the instantaneous cross sectional area of the CSF flow path, \(\dot{P}\) and \(\mu\) are the hydrostatic pressure and axial velocity averaged over the cross-section, \(\dot{P}\) and \(\mu\) are the density and dynamic viscosity of the fluid, \(\psi\) is the rate of CSF generation per unit volume, \(K_{\text{head}}\) is the strictly positive coefficient representing viscous friction resistance of the flow from the unit length of the tube surface, \(K_{\text{head}}\) is the strictly positive head loss coefficient relating to the pipe bend, \(\text{sign}\) is the sign function which extracts the sign of its argument, dot above the variable means the time derivative, prime derivative by the axial coordinate. The input data were taken from previously published studies (3, 6, 9). The details of the utilized numerical scheme of the second order of accuracy in time and space are described in our previous work (10).

CSF production in choroid plexuses of the 4 ventricles was specified as a boundary condition for the model in Equation [2]:

\[
m_{\text{bulk}} = \frac{600 \text{mL}}{\text{day}}
\]

\[
m_{\text{pulse}}(t) = \alpha \left[ \sin(\omega t - \frac{\pi}{2}) - 0.5 \cos(\omega t - \frac{\pi}{2}) \right]
\]

The other source of production from capillary ultrafiltrate spaces was accounted for by the mass conservation equation. The primary CSF absorption sites (i.e., arachnoid granulations) were treated as the outlet boundary conditions (Fig. 1B). For our model, we established a low pulse wave to represent patients with a CF-LVAD (7). A representative transcranial Doppler ultrasound waveforms and M-mode readings of blood flow in the Circle of Willis for a patient with CF-LVAD shown in Figure 1C demonstrates approximately constant flow as expected. We then performed computational fluid dynamic simulations for our 1-dimensional FSI model, which represents the CSF circulation system to predict intracranial pressures and flow rates.
Results

Utilizing boundary conditions with a diminished pulse to represent conditions in a patient with a CF-LVAD, we modeled the pressure and velocity through the cerebral arteries at various locations. Computational simulation of CSF pressure and velocity at the third ventricle (Fig. 2A) and arachnoid granulation (Fig. 2C) demonstrates that the amplitude of pressure and velocity are reduced, but the overall flow rate remains unchanged. Velocity and pressure profiles in the longitudinal direction of CSF flow at the boundaries obtained at the third ventricle are also demonstrated in Figure 2B.

Discussion

Our 1-dimensional FSI model for the investigation of CSF dynamics in patients with CF-LVADs is an original application within this clinical environment. Utilizing the model, we were able to predict the amplitude changes for velocity and pressure of CSF for a patient with a CF-LVAD with presumed low arterial pulse, which did not reveal an overall effect on flow rate. The preservation of CSF flow rate likely results from the continuous-flow circulatory support provided by the LVAD.

The current coupled hydrodynamic model describing CSF flow (1) is based on Reymond’s equation, which requires pulsatility as a precondition (6). Because very little CSF truly circulates through the subarachnoid space, pulsatile flow, rather than bulk flow, is what can be measured on phase contrast magnetic resonance imaging (PC MRI) and is what is currently being utilized by Reymond’s equation (2). However, the pulsatile flow component and in vivo-based transfer function utilized by the model to relate cerebral blood flow to CSF pulsation (1) is no longer applicable when pulsatility is extremely diminished.
According to the above model, continuous-flow circulation would result in an abnormal CSF flow, and as a consequence, in abnormal CSF pressure and accumulation of toxic metabolites. Theoretically, this would then lead to neurologic manifestations such as hydrocephalus, syringomyelia or Chiari malformations (5). However, as patients with a CF-LVAD remain neurologically asymptomatic, the role of pulsatility in the existing model of CSF flow may be overemphasized without accounting for the compensatory changes in CSF production and absorption. Recent research efforts have demonstrated that the traditional physiology of CSF circulation is more complex than previously thought, and includes the role of lymphatic pathways for drainage of CSF along astrocytes, aquaporin channels, and fluid exchange between CSF and interstitial spaces. The current model for understanding CSF circulation via FSI does not take into account these nuances of CSF flow circulation, and thus the model does not appear to be valid in nonphysiologic states such as those of patients with CF-LVADs.

An improved understanding of the CSF circulation has important clinical relevance to understanding CSF-related pathologies such as neurodegenerative, immunological and cerebrovascular disorders of the brain and spinal cord. It may also aid in improving shunt design for hydrocephalic patients and improving methods of CSF-mediated intrathecal and intraventricular drug delivery (3, 6).

At present, there is much to learn regarding the coupled relationship of the CSF system and cardiovascular system. Our preliminary analysis reveals that simplified cylindrical FSI models do not provide an accurate representation of CSF flow and suggests that a more advanced model with complex geometry is needed to account for the flow generation and absorption at each boundary site. Furthermore, it would be important to extend the FSI model to include bidirectional fluid exchange with the extracellular space, perivascular flow and lymphatic drainage for a more comprehensive picture of CSF flow. Radionuclide cisternography or single photon emission tomography/computed tomography (SPECT/CT) (11) and direct and indirect CSF pressure measurement strategies (12) may yield insight into the CSF pressure changes in continuous flow as compared to pulsatile flow conditions. Comparison of CSF cells, viscosity, electrolytes, metabolic, hormonal, blood-brain barrier and EEG changes observed among patients with neurologic pathology (13), healthy individuals, and those with CF-LVADs may explain the adaptive changes that occur in patients with CF-LVADs to compensate for the reduced pulsatility and maintain CSF flow. Together, these may lead to a computational model of mechanical behavior of the CSF system that can be constructed using 3D printing technology to couple the cardiovascular pulse flow with a CF-LVAD in vitro.

Conclusions

The CSF circulation is more complex than previously understood. These findings are applicable to disease conditions in patients with CF-LVADs and suggest that the leading theory of CSF flow is not an optimal representation of CSF flow in this patient population. More studies are needed to elucidate the role of pulsatility in CSF flow and the compensatory changes in CSF production and absorption that occur in CF-LVADs patients with diminished pulsatility.

Disclosures

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