International Journal of Pure and Applied Mathematics
Volume 32 No. 1 2006, 23-32

ON THE PRESSURE DEPENDENCE OF A STARLING-LIKE RESISTOR

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Abstract: A Starling resistor in models of fluid flow through a collapsible tube is a resistance term that depends on the transmural pressure across the tube wall. In a traditional Starling resistor, negative transmural pressure implies that the tube is fully collapsed and fluid flow is blocked. The present work develops a nonlinear expression for a Starling-like resistor that can be used to represent flow resistance in vessels, such as the intracranial transverse venous sinuses, where transmural pressure is negative in the normal resting state and the vessel is not fully collapsed. Expressing flow resistance in terms of vessel cross-sectional area, the lumped resistance between two points in the vasculature subjected to negative transmural pressure is found to depend on

Received: June 5, 2006

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the transmural pressure at the downstream location. Applications to lumped-parameter models for idiopathic intracranial hypertension are discussed.

AMS Subject Classification: 92C35
Key Words: Starling-like resistor, mathematical models, negative transmural pressure, idiopathic intracranial hypertension, transverse sinuses

1. Introduction

In models of fluid flow through collapsible vessels, a Starling resistor or vascular waterfall is a resistance term that increases as the transmural pressure across the vessel wall decreases (Munis and Lozada [12]). When transmural pressure is large, the vessel is considered open and the resistance to flow is small. Conversely, if the transmural pressure is small or negative, then the vessel is partially or completely collapsed resulting in a large (or possibly infinite) resistance. A classic use of a Starling resistor occurs in the lumped-parameter model of intracranial hydrodynamics described by Ursino [17]. In this study, a Starling resistor that depends on upstream transmural pressure is placed at the location where the cerebral veins empty into the saggital sinus near the cerebral lacunae. A Starling resistor at this location is also present in the models developed by Czosnyka et al [4], and Piechnik et al [15]. Further downstream, Pedley et al [13] suggest a similar phenomenon in the jugular vein of the giraffe. A common feature of these locations is that the transmural pressure is positive in the normal resting state. If, in the normal resting state, the transmural pressure at a location is negative, a traditional Starling resistor cannot be introduced as it would imply that the vessel at that location is fully collapsed and flow is totally obstructed in the normal state. Consequently, vessels with negative transmural pressure such as the transverse sinuses have previously been assumed rigid in order to prevent collapse and have been modeled using a constant resistance term.

The assumption of constant resistance for a rigid transverse sinus can be justified in models of normal intracranial physiology. However, this assumption is not appropriate in the case of pathological conditions such as idiopathic intracranial hypertension (IIH). This condition, also called pseudotumor cerebri and benign intracranial hypertension, is a syndrome of unknown cause characterized by elevated intracranial pressure (ICP) without evidence of ventricular dilatation, mass lesion, cerebrospinal fluid (CSF) abnormality, or dural sinus thrombosis (Friedman and Jacobson [5]). Symptoms of IIH include headache, papilledema, and visual obscurations (Binder et al [3]). Untreated, IIH can

Figure 1: Oblique lateral subtracted venogram of the lateral sinuses of an IIH patient showing a stenosis (arrows) in the left transverse sinus. The right transverse sinus is hidden from view in this image. From Higgins et al [8].

cause visual impairment and blindness(Wall and George [18]). In most patients suffering from IIH, a stenosis or tapering of the lateral sinuses is observed by magnetic resonance venography or retrograde catheter venography (Baryshnik and Farb [1], Higgins and Pickard [9], and King et al [10]). A venograph obtained by Higgins et al [8] showing such a stenosis in the left transverse sinus is displayed in Figure 1. The presence of this feature in IIH patients suggests that the transverse sinuses are not completely rigid in individuals at risk for the development of this syndrome (Bateman [2]).

This paper develops a Starling-like resistor for flow through a vessel capable of some degree of collapse at a location where the transmural pressure is negative. The expression for this resistance term is such that the flow resistance is positive and remains bounded despite the negative transmural pressure. Resistance increases as the transmural pressure becomes more negative. Unlike the traditional Starling resistor, the resulting lumped resistor is found to depend on transmural pressure at a downstream location.

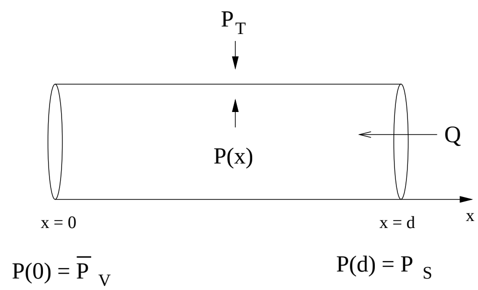

Figure 2: A schematic of the transverse sinus(es). The internal pressure ($P(x)$) is a function of distance (x) upstream from the central venous reference point. The saggital sinus reference point is assumed to be represented at $x = d$. The flow through the vessel(s) is a constant Q due to cerebral autoregulation.

2. The Starling-Like Resistor

Figure 2 shows a section of a circular compliant tube of length d and radius $r(x)$ that models a section of the transverse sinus. The flow Q through this vessel is from right to left, which places the central venous reference point at the origin $x = 0$ and the saggital sinus reference point at the upstream location $x = d$. The reason for choosing this orientation for the flow, as opposed to a more common left to right depiction, will be noted later in this section. Consistent with cerebrovascular autoregulation, Q will be assumed constant.

Pressure in the vessel $P(x)$ is taken to be a function of the upstream distance x from the central venous reference point. The vessel passes through an environment with ambient pressure P_T. Indicative of the sinus vessels passing through the intracranial region, the ambient pressure P_T is assumed independent of x. Pressures at the origin and upstream reference points are given by $P(0) = \overline{P}_V$ and $P(d) = P_S$. Further, it is not assumed that $P_T \leq P(x)$ for $0 \leq x \leq d$, so the transmural pressure $P(x) - P_T$ need not be positive for this vessel.

If $\mathcal{R}(x)$ is the flow resistance in the vessel at position x, then $\mathcal{R}$ can be represented as the pressure gradient at x divided by the cross-sectional flow. In terms of differentials, $\mathcal{R}(x)$ is now related to the pressure $P(x)$ through the equation

$$\mathcal{R} = \frac{dP/dx}{Q}\,, \quad \text{or} \quad \frac{dP}{dx} = Q\mathcal{R}\,, \tag{1}$$

where Q is constant.

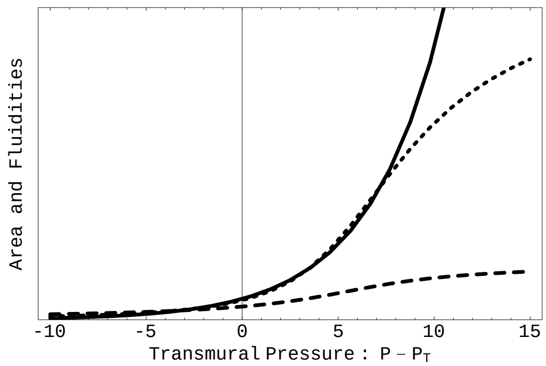

Figure 3: Dashed curve: The cross-sectional area of an artery as described by Langewouter's formula [11]. Dotted curve: The square of the cross sectional area, which is proportional to the fluidity. Solid curve: The exponential approximation to the fluidity.

Flow resistance is a function of cross-sectional area and this area is dependent upon transmural pressure. Depending on the elastic properties of the vessel this relationship can take various forms. In the healthy state, the sinus vessels can be modeled as rigid, or at least rigid enough to sustain significant negative transmural pressures without collapse.

There appears to be no clinical data that relates intracranial venous sinus pressures to cross sectional area in either the healthy or pathological case. However, such a relationship has been developed for the large arteries [11] and involves an arctangent formula in the transmural pressure $P(x) - P_T$. While recognizing that the large arteries are much more rigid than veins, this artangent formula, depicted by the dashed curve in Figure 3, will be used here as the relationship for a semi-collapsible sinus.

The shape of transverse sinuses is fairly circular (Figure 1) and the flow through these vessels is relatively slow and steady compared to arteries. Therefore Poiseuille's law, which relates radius and resistance, may be consistently invoked. For a circular cross-section, the radius $r(x)$ is proportional to the square root of the area. By Poiseuille's law the resistance to flow through the vessel in Figure 2 will now be proportional to the fourth power of the inverse of the radius. It is convenient to rephrase this relationship in terms of the fluidity, $\mathcal{Z}(x)$, which is the inverse of the resistance $\mathcal{R}(x)$. It now follows that the fluidity through the vessel at x will be proportional to the square of the cross-sectional area at that location. The resulting relationship between fluidity and transmural pressure is depicted by the dotted curve in Figure 3.

In the differential equation (1), it is somewhat awkward to use a representation for fluidity that involves a square of an arctangent formula. However, since, for the vessel modeled here, the ambient pressure is generally greater than or equal to the internal vessel pressure, transmural pressures will either be non-positive or positive but small. For such values, the fluidity may be well approximated by an exponential function of the form

$$\mathcal{Z}(x) = B_1 e^{\alpha(P(x)-P_T)}. \tag{2}$$

This approximation is depicted by the solid curve in Figure 3 and leads to a resistance term defined by a function of the form

$$\mathcal{R}(x) = Be^{-\alpha(P(x)-P_T)}, \tag{3}$$

where B in (3) is the inverse of the constant B_1 in (2).

Substituting $\mathcal{R}$ from equation (3) into equation (1) now yields the differential equation

$$\frac{dP}{dx} = QBe^{-\alpha(P-P_T)}. \tag{4}$$

The solution of this equation is

$$P(x) = \frac{1}{\alpha}\ln(\alpha QBx + C) + P_T, \tag{5}$$

where C is a constant of integration to be determined by an appropriate boundary condition.

Two possible choices for the required boundary condition are $P(0) = \overline{P}_V$ or $P(d) = P_S$. However, from the data presented by King et al [10], and in agreement with the waterfall analogy presented by Permut and Riley [14], the down-stream pressure is unaffected by the ambient CSF pressure or the induced stenosis of the sinus. Therefore, the natural boundary condition to impose in (5) is $P(0) = \overline{P}_V$, which motivated both the choice of the downstream venous sinus reference point as the origin and adoption of a right to left flow orientation in Figure 2. Imposing this boundary condition in (5) gives

$$P(x) = \frac{1}{\alpha}\ln\left[\alpha QBx + e^{\alpha(\overline{P}_V - P_T)}\right] + P_T. \tag{6}$$

An expression for the pressure $P_S = P(d)$ at the saggital sinus reference point now follows by evaluating (6) at $x = d$. Consistent with intracranial physiology, (6) implies that the upstream pressure in the vessel $P(x)$ for $0 \leq x < d$ will always be greater than the pressure $\overline{P}_V$ at the down-stream reference point.

3. Applications to Lumped-Parameter Models of IIH

Lumped parameter models provide an attractive method for studying complex physiological systems. In this modeling approach, the system is subdivided by physical constituent into a number of interacting compartments. Fluid flows and volume adjustments are related to pressure differences between adjacent compartments by defining lumped resistance and compliance parameters.

For the flexible vessel depicted in Figure 2, the lumped resistance R between $x = 0$ and $x = d$ is defined by

$$R = \frac{P(d) - P(0)}{Q}. \tag{7}$$

Thus, by (6) a representation for the lumped resistance between the saggital sinus and central venous reference points is given by

$$R = \frac{1}{Q}\left[\frac{1}{\alpha}\ln(\alpha QBd + e^{-\alpha(P_T - \overline{P}_V)}) + (P_T - \overline{P}_V)\right], \tag{8}$$

where α, Q, B, and d are constant parameters. The lumped resistance associated with the Starling-like resistor is thus a positive, increasing function of $P_T - \overline{P}_V$, the negative of downstream transmural pressure.

Computational and experimental results by Heil [7] indicate that, after sufficient external pressure is applied to instigate tube compression, consistent with (8) lumped resistance will be increasing with respect to the negative of the downstream transmural pressure. As with the sinuses modeled here, the tube used by Heil [7] was capable of withstanding nominal negative transmural pressures prior to collapse. Computational results in that study were obtained by numerically solving the steady three-dimensional Stokes equations that approximate the Navier-Stokes equations for slow viscous flow in the tube. Deformation of the tube was described by geometrically nonlinear shell theory. Solving these equations within the complex geometry of actual intracranial vasculature is not practical. By contrast, lumped-parameter models, by accepting limitations on detailed spatial information, allow physiological systems with multiple interacting components to be investigated in a consistent and realistic manner.

A lumped parameter model that embeds the intracranial system in whole-body physiology has been developed by Stevens et al [16] to study the etiology of IIH. This model uses a simplified piecewise-linear version of equation (8) for a lumped resistance term at the level of the transverse sinuses that is a function of the downstream transmural pressure. With such a resistor present, the pathologies of IIH with a stenosed sinus are fully explained by the existence of multiple stable steady-state solutions of the model's governing differential equations. One stable steady state has elevated intracranial pressures and a stenosis indicative of IIH, and numerical simulations match favorably with clinical data. No such steady-state exists if a more traditional upstream Starling resistor is at the venous sinus level. The choice of downstream transmural pressure dependence in the Starling-like resistor, rather than upstream transmural pressure dependence as in the more traditional Starling resistor, was motivated by the results of Grotberg and Jensen [6] where a flexible vessel with internal flow collapses at the furthest downstream location when subjected to increasing ambient pressure. Use of an upstream oriented dependence was further precluded by the fact that when an upstream resistor is present in a lumped parameter model, steady-state vessel pressures must exceed the ambient ICP in order for cerebral blood flow to continue (Ursino [17]). However, clinical data does not support this conclusion with regards to the venous sinuses (King et al [10]). Equation (8) now provides additional theoretical justification for the use of a downstream pressure-dependent Starling resistor in lumped-parameter models of human intracranial fluid dynamics.

Acknowledgments

This work was supported in part by NASA under cooperative agreement NCC5-581.

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