Carotid Sinus as a Mechanotransducer of Shear Oscillation

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Research note

Keywords: Carotid sinus, wall shear stress, homeostasis, cardiovascular, blood flow

Posted Date: July 3rd, 2019

DOI: <https://doi.org/10.21203/rs.2.11025/v1>

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Abstract

Objective The carotid sinus is a region in the cardiovascular system where flow characteristics are transduced by the autonomic nervous apparatus to help maintain cardiovascular homeostasis. The objective of this study is therefore to determine whether the carotid sinus acts as a mechanotransducer of wall shear stress oscillation. **Results** By utilizing magnetic resonance angiograms of undiseased carotid bifurcations, computational fluid dynamic simulations of blood flow were constructed. Employing boundary conditions meant to emulate normal blood flow at rest, the oscillatory shear index (OSI) was tabulated and mapped. The areas of highest OSI were well-isolated in the regions of the carotid bifurcations generally considered to comprise the carotid sinus.

Introduction

The Endothelium as a Mechanotransducer

Vascular endothelium is a dynamic system responsible for both local and systemic control of many functions involved in autonomic homeostasis. As the intermediary between the flow of blood and vascular walls, the endothelium has many functions [1] but perhaps the most significant one is transduction of hemodynamic information from the blood to the underlying vessel wall [2].

The Anatomy and Physiology of the Carotid Sinus

Recent focus on treatments of recalcitrant hypertension, heart failure, and insulin resistance has sparked interest in the anatomy and physiology of the carotid sinus[3]. Particularly, the anatomy of the carotid sinus nerve (CSN), with extensive communications between the sympathetic and parasympathetic fibers along its course from the skull base to the dilated portion of the origin of the internal carotid artery just distal to the common carotid bifurcation, supports its role as a substrate for the complex mechanisms by which the body maintains cardiovascular homeostasis. From the earliest descriptions in the 1950's[4], the literature describes the "baroreceptor" role of the carotid sinus, as that is clinically measurable and thereby relevant. The importance of blood pressure control for so many fields in medicine means the complexities of blood pressure homeostasis remain a much studied area.

The Carotid Sinus as a Mechanotransducer of Shear Oscillation

The location of the CSN makes it well suited to transducing flow characteristics only possible in an area such as the carotid sinus – namely just distal to a bifurcation in an area above the heart at an immediate tributary just off the left ventricular outflow tract. Flow at a bifurcation allows for breakup of the smooth laminar flow, and the eddies created result in shear forces that can be directed, and therefore detected, at the vessel wall. To do so at the base of the internal carotid is appropriate when considering the

distribution of blood flow between the external and internal carotid arteries, as noted by Sato and colleagues[5]. They found that, compared to rest, the blood flow in the internal carotid remained somewhat close to baseline whereas in the external carotid blood flow increased proportionally with increased common carotid blood flow. This phenomenon of maintaining internal carotid flows at baseline levels even in the setting of doubling cardiac work, supports the role of the carotid sinus as part of the cardiovascular homeostatic apparatus.

Therefore, the aim of this study is to examine if normal blood flow present at the carotid sinus allows it to be suitable as a sampling site for transduction of shear stress oscillation. Our hypothesis states that if the areas of increased shear stress oscillation in normal carotid bifurcations coincides with sites where the CSN is seen to enter the vessel wall of the internal carotid, then the carotid sinus may be acting as a mechanotransducer of wall shear oscillation.

Methods

In this study, numerical simulations of blood flow in normal human carotid bifurcations were carried out to evaluate the wall shear characteristics in the region where the CSN is noted to insert into the wall adventitia. The blood is assumed to be incompressible Newtonian fluid. The Virtual Flow Simulator (VFS) code [6] is employed to simulate the blood flow in the carotid bifurcation. In VFS the blood flow is governed by the following incompressible Navier-Stokes equation and continuity equation:

[Formula could not be included here. It can be found in the "Formulas" supplemental file. See there also for missing characters denoted below by *** This is formula 1]

where *** the fluid density, *** is the blood velocity, *** is the time, *** is the pressure, *** is the dynamic viscosity. In the present work, ***, and ***. The geometry of the carotid is represented using the immersed boundary (IB) method [7]. The wall of the carotid is assumed to be rigid.

The velocity boundary condition with the waveform from Holdsworth et al. (1999) (Figure 1) and a parabolic distribution is specified at the inlet plane of the common carotid artery. The Neumann boundary condition is applied at the outlet of the internal carotid artery. At the outlet of the external carotid artery, the flow rate is fixed at 26% (Marshall et al. 2005) of that applied at the inlet and the velocity distribution is given by that at interior points next to the outlet plane. In all cases, grid nodes are uniformly distributed in all three directions with the grid spacing 0.1 mm. A grid of spacing 0.2 mm was shown to be sufficient to resolve the wall shear stress (Moyle et al., 2006). The size of time step varies in time with the CFL number fixed at 0.8.

In simulations the carotid geometry, which is discretized using triangular meshes, is obtained based on magnetic resonance angiograms performed on patients admitted to Stony Brook Medical Center who underwent scans as part of an institutional stroke imaging protocol. The angiograms images were reviewed and obtained after approval by the institutional review board. Eleven angiograms were randomly selected for review from scans performed over a three month period in 2018. These images were

reviewed anonymously. The criteria for selection included 1) that the images had to be obtained utilizing the same imaging protocol on the same scanner, 2) the angiograms had to be free of disease or filling defects of any kind, 3) the images themselves had to be sufficiently free of motion artifact, and 4) the patients had to be adults, the images had to be of the right carotid bifurcation. Of these initial scans, six met the criteria (1 female, 5 males) and were processed to create the mesh for simulation. To process each scan, 3D-TOF MRA data was cropped from the region containing the bifurcation. The 3D data was reconstructed using open-source software 3D-Slicer 4.8.1[8] (www.slicer.org) in order to create a volume rendering. This rendering was imported into a stereolithography (STL) file and then used to create the grid.

The wall shear stress (WSS) results were calculated and rendered using a WSS map (Figure B.) and the oscillatory shear index (OSI) was then derived using the following equation:

[Formula could not be included here. It can be found in the "Formulas" supplemental file. See there also for missing characters denoted below by *** This is formula 2]

where *** represents the WSS vector and T represents the period of the cardiac cycle

(Figure C.). It is a metric that depicts how aligned with the vector of greatest WSS is with the primary flow. An OSI of 0 suggests no change of direction between the WSS and the primary flow. An OSI of 0.5 suggests a complete change of direction. It is a means of quantifying the magnitude of change of direction of WSS.

Results

On visual inspection, the WSS results for the six carotids chosen resulted in WSS patterns that isolated the region where the CSN is understood to insert into the adventitial layer of the carotid artery. In the area of recirculation where the base of the internal carotid dilates, the change in direction of the flow results in WSS patterns that resulted in regions of shear that are consistent with less laminar flow, an example of which is depicted in Figure B. As the direction of flow is directed away from the endothelium, the WSS decreases as the vectors of flow are directed away from vessel wall.

Qualitatively, when OSI is tabulated for the six carotids, the areas of greatest change of direction of WSS overlaps the regions understood to comprise the carotid sinus. Values for OSI in areas outside the sinus region were largely at or near zero. The region at the origin of the internal carotid where the vessel is dilated has the highest values for OSI, with values at or near 0.2 (Figure C). This was seen in all six carotids.

Discussion

Initiators and transducers of vascular endothelial have been studied extensively. The importance of vascular endothelial function for homeostasis in various organ systems cannot be overstated; it spans

cardiac[9], pulmonary[10], renal[11], hepatic [12], and other functions. This pervasive significance of endothelial function cannot be achieved without its ability to transduce and transmit local flow information to the organs surrounding the blood vessel. The process starts with transduction of local mechanical blood flow data, particularly wall shear stress, or mechanotransduction[13]. These blood flow characteristics are then transmitted to the surrounding vessel wall and parenchyma by the cytoskeletal anatomy of the cells which transmits wall shear forces across cells as well as by plasma membrane proteins, mechanosensitive ion channels, and abluminal cell surface adhesions [1]. These, in turn, utilize G-protein, Mitogen, and other intracellular pathways to transmit this data to broadcast it to subsequent cells along a specific pathway meant to effect a particular function. In this way, the autonomic nervous system consolidates this data from various sites where blood flow information is transduced to create a cohesive homeostatic system optimizing functioning and blood flow across various organ systems.

The location and shape of the sinus and its nerve at the base of the internal carotid is unique for a number of reasons. The dilated segment at the base of the internal carotid allows for an area of “recirculation”[14]. This area of recirculation where the laminar flow in the common carotid yields to regions of flow reversal creates a number of eddies and areas of vortical flow. To characterize the area of recirculation, observers have used methods such as computational fluid dynamics (CFD) and ultrasound[15]. Furthermore, the CSN is described as sending neuronal endplates between the adventitial and endothelial layers of vessel wall that comprise the base of the internal carotid[16]. These regions appear to encompass the areas of non-laminar flow.

Our study shows that the areas of highest OSI qualitatively correlate well to the areas where the CSN is understood to be located within the adventitia of the carotid bifurcation. The lower values of OSI in the regions excluding the carotid sinus support the notion that the flow shear characteristics are unique to the sinus region. When framing the discussion of the physiology of the carotid sinus, it is referred to as a baroreceptor, in part, because blood pressures can be directly measured in the experimental setting. By recasting the understanding of the carotid sinus as a mechanotransducer of WSS, we as clinicians may be closer to understanding what the autonomic nervous system is directly measuring. This suggests the possibility that future studies can focus on measurable parameters known to alter the shear characteristics of blood flow. Anesthesiologists can include “endothelial function” in the list of end-organ function (along with cardiac, pulmonary, and renal functions) considered in the calculus of proper perioperative resuscitation. Therefore “normal” OSI, or some proxy thereof, may represent a clinical end-point against which we can consider fluid and blood management in the clinical setting when assessing cardiovascular homeostasis.

Limitations

The small sample size may contribute to a lack of generalizability of the hypothesis that the carotid sinus may be a mechanotransducer of flow shear oscillation. Furthermore, the gender distribution of the subjects in the study may suggest that the OSI may isolate the CSN region well in males but not

necessarily in females. Also, since the vessel diameter in males is larger when compared to females, the effect on shear oscillation and the relative effects of viscosity on the region of recirculatory flow has to be considered.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of Stony Brook University School of Medicine. (Protocol number 1340636-3) This study met criteria for waiver of consent in order to review records that already exist.

Availability of data and material

Not applicable.

Funding

There is no external source of funding for this study.

Acknowledgements

The authors would like to thank the radiology technicians at Stony Brook University Medical center who were instrumental in the acquisition and processing of the original magnetic resonance images.

Consent for publication

Not applicable.

Competing Interests

Not applicable.

Authors contributions

AI: Review of the literature, concept and design, interpretation of data, drafting of manuscript. XY: review of literature, design and implementation of simulations, contribution of methods with respect to simulations, interpretation of data, critical review of manuscript.

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Figures

Figure A.

A.

Figure 1

Figure A. Blood flow rate utilized for boundary conditions over one cardiac cycle at a rate of 60 beats per minute. The red circle denotes rate at peak systole.

B

Figure 2

Figure B. B. Wall shear stress (WSS) map at the moment of peak systole of carotid “1” in Figure C. ICA = Internal carotid artery. ECA = External carotid artery. CS = Carotid sinus region. CCA = Common carotid artery.

C

Figure 3

Figure C. C. Oscillatory Shear Index (OSI) map of six normal carotids. Values closer to 0 ("Low OSI") are regions where laminar flow disruption is minimal. Values closer to 0.5 ("high OSI") are regions where flow deviates most from main direction of flow. ICA = Internal carotid artery. ECA = External carotid artery. CS = Carotid sinus region. CCA = Common carotid artery.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Formulas.pdf](#)