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Influence of aging-induced flow waveform variation on hemodynamics in aneurysms present at the internal carotid artery: A computational model-based study

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ABSTRACT

The variation of blood flow waveform in the internal carotid artery (ICA) with age is a well-documented hemodynamic phenomenon, but little is known about how such variation affects the characteristics of blood flow in aneurysms present in the region. In the study, hemodynamic simulations were conducted for 26 ICA aneurysms, with flow waveforms measured in the ICAs of young and older adults being used respectively to set the inflow boundary conditions. Obtained results showed that replacing the young-adult flow waveform with the older-adult one led to little changes ($< 10\%$) in simulated time-averaged wall shear stress (WSS), transient maximum WSS, relative residence time and *trans*-aneurysm pressure loss coefficient, but resulted in a marked increase ($32.36 \pm 17.24\%$) in oscillatory shear index (OSI). Frequency-domain wave analysis revealed that the progressive enhancement of low-frequency harmonics dominated the observed flow waveform variation with age and was a major factor contributing to the increase in OSI. Cross-sectional comparisons among the aneurysms further revealed that the degree of increase in OSI correlated positively with some specific morphological features of aneurysm, such as aspect ratio and size ratio. In summary, the study demonstrates that the variation in flow waveform with age augments the oscillation of WSS in ICA aneurysms, which underlies the importance of setting patient-specific boundary conditions in hemodynamic studies on cerebral aneurysms, especially those involving long-term patient follow-up or cross-sectional comparison among patients of different ages.

1. Introduction

Aging is a common risk factor for vascular diseases. It has been well established that the vascular system is subject to progressive structural degeneration, endothelial dysfunction and myogenic impairment during aging, which independently or jointly increase the susceptibility of vessels to pathological changes [1–4]. In addition, aging-associated vascular changes are usually accompanied by significant hemodynamic alterations [5–9]. For instance, it has been observed that the blood flow waveform in the internal caotid artery (ICA) differs remarkably between young and older adults [10–12]. Following the increase in age, the secondary flow peak appearing in late systole rises gradually, becoming comparable to or even higher than the first systolic peak in advanced age [10,11]. The observation raises a question as to how the aging-induced variation in flow waveform would affect blood flow patterns in the ICA. The effects might have special implications for the assessment of hemodynamics in aneurysms present at the ICA where the local hemodynamic environment has been widely proved to associate with the progression or rupture of aneurysm [13–17]. In particular, it has been found that the prevalence of cerebral aneurysm is comparable among different age groups (> 30 years old) [18] and that an untreated cerebral aneurysm may maintain an unruptured state for long time (e.g., only about 30% of untreated aneurysms ruptured during 30 years' follow-up [19,20]), which implies that the natural histories of most cerebral aneurysms are accompanied by considerable variations in flow waveform with age. Therefore, understanding how flow waveform variation with age affects intra-aneurysmal flow patterns would provide additional information for assessing the risk of

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aneurysm rupture, especially in long-term follow-up studies. To address the issue, a basic step is to quantitatively evaluate the relationship between intra-aneurysmal hemodynamic parameters and the characteristics of flow waveform, which is however challenging for clinical studies due to the limited temporal/spatial resolutions of hemodynamic measurement techniques available in general clinical settings.

As an alternative approach, computational fluid dynamics (CFD) simulations have been widely employed to quantify hemodynamic parameters in cerebral aneurysms [21–27]. In the present study, we performed hemodynamic simulations on 26 ICA aneurysms using two typical flow waveforms measured in young and older adults respectively, aiming to elucidate how aging-related flow waveform variation affects the characteristics of intra-aneurysmal flow patterns. Moreover, the flow waveforms were analyzed in the frequency domain to explore the dominant wave components behind the observed waveform difference between young and older adults and their contributions to the changes of simulated flow patterns in the aneurysms.

2. Materials and methods

2.1. Variation of ICA flow waveform with age

To investigate the variation of ICA flow waveform with age, population-averaged data were derived from previous in vivo studies [10,11] where time-resolved volumetric flow waveforms in the ICAs were measured in young normal adults and older adults (with little or no carotid artery disease) using the gated phase-contrast magnetic resonance imaging technique. The normalized flow waveforms (all have a mean flow rate of 1.0) reported in Refs. [10,11] were herein transformed into flow velocity waveforms with a mean value of 0.31 m/s (a value close to that reported in Ref. [28]) by multiplying them by a constant of 0.31 (m/s). In addition, the time lengths of all flow waveforms were fixed at 0.949 s according to the mean heart period measured in old adults [11]. From Fig. 1(a), the variation of ICA flow velocity waveform with age is featured by a rising secondary peak in late systole. Each flow waveform was further decomposed into Fourier series to shed light on the composition of the waveform in the frequency domain,

$$u(t) = u_0 + \sum_{n=1}^{N} U_n \exp(in\omega t), \quad (1)$$

where u_0 is a constant representing the mean flow velocity (i.e., 0.31 m/s), N is the total number of harmonics, U_n is the modulus of the nth harmonic, and ω is the angular frequency.

From the moduli of the first seven harmonics (i.e., U_1 to U_7 in Eq. (1) at frequencies of 1.05, 2.10, 3.15, 4.20, 5.25, 6.30 and 7.35 Hz) (see Fig. 1(b)), it is evident that the moduli of the low-frequency harmonics (i.e., the first and second harmonics) increase progressively with age, which indicates that concentration of harmonic components towards the low-frequency domain is a predominant mechanism behind the observed flow waveform variation with age.

2.2. Geometric and mesh models of the ICA aneurysms

The geometric data of 26 unruptured (at the time of clinical data acquirement) ICA aneurysms were derived from the Aneurisk database [29]. The geometric models of all the aneurysms and adjacent arteries have already been reconstructed from medical images using the Vascular Modeling Toolkit [30] with the data (in STL format) being freely accessible to researchers. In the present study, the original geometric models were slightly modified to simplify hemodynamic simulations by cutting off small arteries (typically those distal to the first bifurcation of the middle cerebral artery or the anterior cerebral artery). However, small arteries close to or stemming directly from an aneurysm (e.g., the ophthalmic artery and the anterior choroidal artery) that might considerably affect intra-aneurysmal hemodynamics were retained. In addition, to reduce potential influences on the simulation of intra-aneurysmal hemodynamics from artifacts introduced by the prescription of outflow boundary conditions, the outlets of each model were extended outward along the normal directions by adding extension tubes. The lengths of extension tubes were set to be 20 and 10 times of the corresponding outlet diameters for major cerebral arteries (e.g., the middle and anterior cerebral arteries) and small branch arteries (e.g., the ophthalmic and anterior choroidal arteries), respectively. Our numerical test on an aneurysm model demonstrated that further doubling the lengths of the extension tubes only had minor influence on the results of hemodynamic simulation (e.g., the change in spatially averaged wall shear stress of the aneurysm sac was less than 0.1%). The geometric models were subsequently processed with a commercial software (ANSYS ICEM CFD 16.0) to generate mesh models to be used in hemodynamic simulations. The entire fluid domain of each model was firstly divided by tetrahedral elements with a minimum size of 0.045 mm, and subsequently a mesh refinement treatment was implemented by creating five layers of prism elements along the vascular walls to help improve the precision of flow computation in the near-wall regions (see Fig. 2(b)). Numerical experiments conducted for three representative models demonstrated that reducing the minimum mesh size from 0.045 mm to 0.035 mm led to less than 1% changes in simulated mean wall shear stresses in the aneurysm regions. Therefore, the adopted mesh density was considered sufficient to yield numerically acceptable results. The total number of elements contained by each mesh model ranged from 3 to 10 million depending on the size and geometry of the model.

2.3. Hemodynamic simulation

Blood flows were modeled as an incompressible Newtonian fluid governed by the unsteady Navier-Stokes equations. The density and

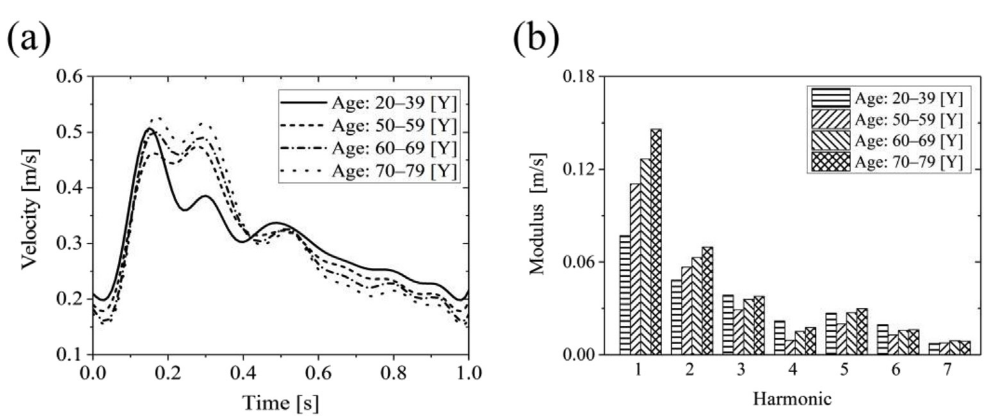

Fig. 1. Flow velocity waveforms in different age cohorts (a) and corresponding harmonic moduli (b). The data of the '20–39' age cohort and those of the other three age cohorts are derived from Ford et al. [10] and Hoi et al. [11], respectively. It is noted that the original flow rate data reported in Refs. [10,11] have been herein transformed into flow velocity data with all resulting flow velocity waveforms having a uniform mean value of 0.31 m/s. 'Y' is the abbreviation of 'years old'.