In vivo three-dimensional blood velocity profile shapes in the human common, internal, and external carotid arteries

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In vivo three-dimensional blood velocity profile shapes in the human common, internal, and external carotid arteries

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Objective: True understanding of carotid bifurcation pathophysiology requires a detailed knowledge of the hemodynamic conditions within the arteries. Data on carotid artery hemodynamics are usually based on simplified, computer-based, or in vitro experimental models, most of which assume that the velocity profiles are axially symmetric away from the carotid bulb. Modeling accuracy and, more importantly, our understanding of the pathophysiology of carotid bifurcation disease could be considerably improved by more precise knowledge of the in vivo flow properties within the human carotid artery. The purpose of this work was to determine the three-dimensional pulsatile velocity profiles of human carotid arteries.

Methods: Flow velocities were measured over the cardiac cycle using duplex ultrasonography, before and after endarterectomy, in the surgically exposed common (CCA), internal (ICA), and external (ECA) carotid arteries (n = 16) proximal and distal to the stenosis/endarterectomy zone. These measurements were linked to a standardized grid across the flow lumina of the CCA, ICA, and ECA. The individual velocities were then used to build mean three-dimensional pulsatile velocity profiles for each of the carotid artery branches.

Results: Pulsatile velocity profiles in all arteries were asymmetric about the arterial centerline. Posterior velocities were higher than anterior velocities in all arteries. In the CCA and ECA, velocities were higher laterally, while in the ICA, velocities were higher medially. Pre- and postendarterectomy velocity profiles were significantly different. After endarterectomy, velocity values increased in the common and internal and decreased in the external carotid artery.

Conclusions: The in vivo hemodynamics of the human carotid artery are different from those used in most current computer-based and in vitro models. The new information on three-dimensional blood velocity profiles can be used to design models that more closely replicate the actual hemodynamic conditions within the carotid bifurcation. Such models can be used to further improve our understanding of the pathophysiological processes leading to stroke and for the rational design of medical and interventional therapies. (J Vasc Surg 2011;54:1011-20.)

Atherosclerosis of the carotid artery bifurcation is a leading cause of stroke. Numerous studies link carotid bifurcation disease to the complex flow patterns present in the carotid bulb.1-3 A sound understanding of carotid bifurcation pathophysiology and the design of ideal devices and techniques for treatment of carotid disease require thorough knowledge of the actual hemodynamic properties within the carotid artery. The hemodynamics of the carotid bifurcation are rather complex. The natural widening of the carotid bulb and the branching into the internal (ICA) and external carotid arteries (ECA) perturb the normal laminar flow present in the more proximal common carotid artery (CCA).2,4 Flow alterations occur in both the longitudinal (parallel to the axis of the vessel) and transverse (perpendicular to the axis of the vessel) directions. In the longitudinal direction, flow in the bulb is partially reversed, a phenomenon termed boundary layer separation.2,4 In the transverse direction, flow undergoes considerable rotation, a condition known as secondary flow.2,4 Measurement of blood flow velocity vectors in the bulb is a challenging task because standard duplex examination is aimed to capture the longitudinal component of the velocity vector, providing no information on the transverse component or secondary flow.

Mathematical modeling can be utilized to overcome the complexities of direct hemodynamic measurements in the carotid bulb. Proximal and distal to the carotid bulb, flow is unidirectional with almost no boundary layer separation or secondary flow.4 Duplex ultrasound can accurately and precisely quantify the flow characteristics in these arterial segments and these measurements can be used as inflow (CCA measurements) and outflow (ICA and ECA measurements) boundary conditions for mathematical modeling of flow within the bulb. In addition to the center-luminal velocity, the shape of the velocity profile, its pulsatile characteristics, and geometry of the artery are also required knowledge for accurate modeling. These mathe-
matical models can then be used to calculate and visualize the complex flow conditions within the carotid bulb.

Most mathematical models that have been used to this point have significant limitations. In these models, velocity profiles are usually presumed symmetric about the arterial axis if measurements are made 4 to 5 vessel diameters from the flow divider. Even though it has recently been demonstrated that axisymmetric or fully developed flow appears to be the exception rather than the rule even in presumably straight CCA, typically velocities are still measured at one location in the center of the arterial lumen where flow is assumed to be the fastest. The remainder of the velocity profile is then calculated using axisymmetric parabolic or plug-shaped Womersley-type functions. This method is based on results obtained from idealized mathematical models and experiments using uniform, round, and rigid artificial vessels. However, while idealized geometry may be valuable for understanding certain flow phenomena, the in vivo carotid artery is rarely round, straight, or uniform in diameter. In addition, the geometry of the carotid artery varies from one patient to another. All of these factors may have pronounced effects on the shape of the velocity profiles and must be considered when developing mathematical flow models. The main reason why this assumption is widely used in modeling is lack of data in the literature that would report the details of the skewed shape of the CCA, ECA, and ICA velocity profiles.

We are presenting a systematic and detailed in vivo evaluation of velocity profiles in the human proximal CCA, distal ICA, and distal ECA from a series of patients undergoing carotid endarterectomy. All measurements were performed in vivo, in the surgically exposed carotid arteries before and after endarterectomy. To avoid limitations introduced by center-luminal velocity measurement alone, we measured velocities in nine different locations across the flow lumina of the CCA, ICA, and ECA (Fig 1). For each individual patient, three-dimensional, pulsatile velocity profiles were constructed and used to calculate mean velocity profiles for the preoperative and postoperative CCA, ICA, and ECA. In combination with geometrical data, these profiles can be used as flow boundary conditions for mathematical models studying the hemodynamics of the carotid artery.

METHODS

In vivo blood velocity measurements. The research protocol was approved by the institutional review board of the Veterans Affairs Nebraska-Western Iowa Medical Center and informed consent was obtained from all patients. Duplex ultrasound (Pro Focus 2202, Probe 8809; B-K Medical, Herlev, Denmark) evaluation of carotid artery blood flow was performed in 16 male patients (mean age, 67.9 ± 7.8 years) with severe (>80% diameter reduction) carotid bifurcation occlusive disease. None of the patients

Fig 1. Schematic of a typical carotid bifurcation and locations of the points 1-9 where the velocity waveforms were measured. CCA, Common carotid artery; ECA, external carotid artery; ICA, internal carotid artery.
had previous open or endovascular interventions performed on their carotids. Because of the improved resolution and optimal access to distal segments of the ICA and ECA, we chose to perform our measurements intraoperatively on the carotid bifurcation after it was exposed for the purposes of carotid endarterectomy. After exposure of the carotid bifurcation and control of the CCA, ICA, and ECA, preendarterectomy velocity measurements were obtained. After completion of the endarterectomy, closure of the arteriotomy, and re-establishment of flow, the postendarterectomy measurements were obtained. All patients were supine with arteries immersed in saline such that the ultrasound probe was not in physical contact with the artery during insonation. The systemic blood pressure was always within the normal range during ultrasound measurements. Mean preendarterectomy peak systolic pressure (PSP) was 126 \pm 20 \text{ mm Hg}, and end diastolic pressure (EDP) was 64 \pm 9 \text{ mm Hg}. Mean postendarterectomy PSP was 114 \pm 16 \text{ mm Hg}, and EDP was 58 \pm 6 \text{ mm Hg}. The arteries were fully dissected from surrounding tissues in their anterior, medial, and lateral aspects, and therefore the effect of surrounding tissues in the intraluminal flow velocities of the carotid arteries was not evaluated and was assumed to be minimal. Natural orientation of the carotid artery was preserved during insonation. We used the duplex to ascertain absence of residual stenosis or intimal flaps in CCA, ICA, and ECA prior to performing the postendarterectomy measurements. All operations and measurements were performed by the same vascular surgeon, and all patients received carotid endarterectomy using longitudinal arteriotomy and primary closure. Patients had a mean preoperative stenosis of 90\% (range, 80\%-95\% based on measurements obtained from preoperative computerized tomographic angiography). Preoperative duplex ultrasound evaluation showed mean peak systolic velocity (PSV) of 371 \pm 115 \text{ cm/s} and end diastolic velocity (EDV) of 152 \pm 35 \text{ cm/s}. Mean ICA/CCA ratio was 5.2 \pm 2.3.

For each patient, velocity measurements were performed in three locations. The first location was 40 mm proximal to the flow divider in the CCA, the second in the ICA 50 mm distal to the flow divider, and the third in the ECA 30 mm distal to the flow divider. For the postendarterectomy ICA measurements, the location of the velocity measurements was at least 20 mm distal to end of the arteriotomy closure. These locations were based on data describing the distance from the flow divider where flow reorganizes to become laminar. Chen\textsuperscript{11} and Perktold\textsuperscript{9} report lengths of at least 4 to 5 arterial diameters. As the typical diameter of the common carotid artery is 5 to 8 mm and the usual diameters of the internal and external carotid arteries are 4 to 6 mm,\textsuperscript{12,13} based on these recommendations, velocity measurements should be performed at least 20 to 40 mm proximal to the carotid bulb in the CCA and 16 to 30 mm distal to the carotid bulb in the ICA and ECA. At each of the three locations, velocity waveforms were measured at nine equally spaced points across the anterior-posterior and lateral-medial directions (Fig 1). Measurements in the anterior-posterior orientation were performed with the probe positioned on top of the artery at the center of the anterior wall. The cursor on the duplex device screen was then moved within the lumen from the center to the anterior wall and then down to the posterior wall. Measurements in the lateral-medial orientation were taken by shifting the probe along the anterior wall of the artery laterally then medially, always keeping the cursor equidistance from the anterior and posterior walls of the artery.\textsuperscript{14,15}

**Building three-dimensional velocity profiles.** Blood velocity waveforms were digitized and entered into a specially developed Matlab code that interpolated axial velocity data across the cross-section of the vessel, providing information for precisely describing the full velocity profile. Interpolation was performed with third degree polynomials, ensuring a smooth distribution of velocity along the radial and circumferential directions of the arterial lumen. Thus, for each patient and each carotid branch, pre- and postendarterectomy three-dimensional pulsatile profiles were constructed. Since the length of the cardiac cycle was different for all patients, it was normalized to a 1 s cycle so that the mean velocity profile could be calculated. Similarly, because of differences in the diameters of the arteries, all measurements were scaled to a diameter of 1 cm.

**RESULTS**

**In vivo blood flow profiles in the carotid artery**

Pulsatile velocity profiles in the CCA, ICA, and ECA before and after endarterectomy were constructed from the in vivo duplex ultrasonographic data. Mean velocity profiles calculated from the data obtained from all 16 patients at specific cardiac cycle time points are presented in Figs 2-4. Scheme of the cardiac cycle and time points at which velocity data are presented is provided in each figure. Peak systole (PS) is the time of maximum flow, early diastole (ED) is the time of minimum flow, and late diastole (LD) is the end of the cardiac cycle.

**Common carotid artery**

Mean velocity profiles in the pre- and postendarterectomy common carotid artery are presented in Fig 2.

**Anterior-posterior side**

**Systole.** Peak systolic velocity increases by 15 cm/s after endarterectomy and its profile shape becomes more peaked. Both pre- and postendarterectomy profiles demonstrate higher systolic velocities posteriorly. Postendarterectomy peak systolic values close to the posterior wall are 19 cm/s higher than the velocities close to the anterior wall. This difference reaches statistical significance in the CCA, at peak systole ($P = .036$). Maximum systolic values are detected in the center lumen.

**Diastole.** Diastolic velocity values at late diastole are higher after endarterectomy, while the opposite is observed at early diastole. Early diastolic profiles are skewed toward the anterior wall. Posterior wall velocities however are still higher than anterior wall velocities. This result is statistically significant ($P = .023$) before endarterectomy at late dias-
After endarterectomy profiles become more symmetric. Maximum velocity at early diastole is detected at the mid-distance between the center of the lumen and the anterior wall in both pre- and postendarterectomy conditions. Maximum values at late diastole are seen in the center lumen of the artery.

**Lateral-medial side**

**Systole.** Peak systolic velocity increases by 14 cm/s after endarterectomy, and the profile shape becomes more peaked. Both pre- and postendarterectomy profiles demonstrate higher systolic velocities laterally. The peak systole profile is skewed toward the lateral wall, and its shape changes from M-shaped before endarterectomy to parabolic-like after. Maximum velocities are detected mid-distance between the center of the lumen and the lateral wall.

**Diastole.** Velocity values for late diastole increase after endarterectomy but retain their profile. Velocity values for early diastole decrease after endarterectomy, and their profile becomes more flat with an increase of velocity at the lateral wall. During diastole, the early diastolic velocity profiles are skewed toward the lateral wall while the late diastolic profile remains fairly symmetric. Maximum velocity at early diastole is observed in the center lumen before endarterectomy and moves toward the lateral wall after. Maximum velocity at late diastole is observed in the center lumen both before and after endarterectomy.

**External carotid artery**

Mean velocity profiles in the pre- and postendarterectomy external carotid artery are presented in Fig 3.

**Anterior-posterior side**

**Systole.** Peak systolic velocity decreased by 30 cm/s after endarterectomy. Both pre- and postendarterectomy profiles demonstrate higher systolic velocities posteriorly, but the difference between anterior and posterior values for the postendarterectomy carotid is more pronounced and equals 28 cm/s \((P = .041)\). Maximum systolic values are detected in the center lumen.

**Diastole.** Diastolic velocity values at both early diastole and late diastole are lower after endarterectomy. Before endarterectomy at early diastole, the velocity profile has a peaked shape with higher velocities close to the anterior wall and maximum values in the center lumen. After endarterectomy, the velocity profile changes to the M-shaped with higher velocities posteriorly and maximum values...
observed between the center of the lumen and the posterior wall. Preendarterectomy profile at late diastole is almost flat with slightly higher values anteriorly. After endarterectomy, the profile reverses to the posterior side.

Lateral-medial side

**Systole.** Peak systolic velocity decreases by 30 cm/s after endarterectomy. The velocity profile changes from M-shaped to peaked, with maximum values moving from mid-distance between the center of the lumen and the medial wall preendarterectomy to the center of the lumen postendarterectomy. After endarterectomy, the velocity close to the medial wall is 9 cm/s higher than the velocity close to the lateral wall; however, the profile is skewed to the lateral side.

**Diastole.** Diastolic velocity values at both early diastole and late diastole are lower after endarterectomy than before. Before endarterectomy at early diastole, the velocity profile has a peaked shape with higher velocities close to the medial wall and maximum values in the center lumen. After endarterectomy, the velocity profile changes to a wave-shape with the highest velocities observed close to the lateral wall and mid-distance between the medial wall and the center lumen. Velocity values for late diastole decrease after endarterectomy but retain their profile.

Internal carotid artery

Mean velocity profiles in the preendarterectomy and postendarterectomy internal carotid artery are presented in Fig 4.

**Anterior-posterior side**

**Systole.** Peak systolic velocity increases by 12 cm/s after endarterectomy and its profile becomes more symmetric and spread-out. Both pre- and postendarterectomy profiles demonstrate higher systolic velocities posteriorly. Maximum systolic values are observed in the center lumen.

**Diastole.** Diastolic velocities are higher posteriorly. This is statistically significant for postendarterectomy ICA at late diastole ($P = .043$). At early diastole, the pre- and postendarterectomy velocities are relatively unchanged, with maximum values observed in the center lumen. However, the shape of the velocity profile after endarterectomy changes from peaked to a more symmetric and spread-out appearance. At late diastole, the profile also changes its shape from peaked to more blunt, with maximum velocity values observed at mid-distance between the posterior wall and the center lumen.
Lateral-medial side

**Systole.** Peak systolic velocity increases after endarterectomy. Preendarterectomy the velocity profile is skewed to the lateral side, but postendarterectomy it skews in the medial direction. After endarterectomy the velocity profile becomes more symmetric. Velocity values close to the lateral wall are higher than those near the medial wall for both pre- and postendarterectomy artery. Maximum velocity values are observed in the center lumen.

**Diastole.** Velocities at early diastole are higher laterally than medially, by 13 cm/s and 4 cm/s pre- and postendarterectomy, respectively. Before endarterectomy, the maximum velocity at early diastole is observed at the mid-distance between the lateral wall and the center lumen. Postendarterectomy, at late diastole the velocity increases. After endarterectomy, both end diastolic and late diastolic velocity profiles become more smooth and symmetric, with maximum velocities observed in the center lumen.

**Variability between the patients**

Variability of the velocity profiles between the patients was studied by calculating the standard deviations of the mean velocity profiles plotted on Figs 2-4. For brevity, we present the results only for the postendarterectomy peak systolic and late diastolic measurements. As demonstrated in Fig 5, there is appreciable variability in the velocity profiles between the patients for all three carotid artery branches. However, the main characteristics of the velocity profiles described above are valid for the majority of the subjects.

**Three-dimensional blood velocity profiles**

Three-dimensional blood velocity profiles were constructed from the data presented in Figs 2-4 by interpolating the velocities between each point of measurement (Fig 1). Fig 6 presents the mean three-dimensional peak systolic velocity profiles in the postendarterectomy CCA, ICA, and ECA. As before, the arterial lumen was normalized to a circle 1 cm in diameter. Velocity profiles in all three carotid artery branches were not symmetric about the arterial centerline.

**DISCUSSION**

Despite the well-known association of atherosclerosis with systemic risk factors, lesions tend to occur focally in regions of the arterial tree demonstrating disturbed flow. Numerous studies\textsuperscript{1,16} suggest that certain hemodynamic factors, particularly low and oscillating wall shear stress,
Fig 5. Mean velocity profiles in the lateral-medial and anterior-posterior directions for common (CCA), external (ECA), and internal (ICA) postendarterectomy carotid artery at peak systole and late diastole. Standard deviations are plotted along with mean values to show the variability of data. Horizontal axis represents the diameter of the artery normalized to 1 cm.
contribute to the initial localization of atherosclerotic plaque and to the development of restenosis and treatment failure following operative or percutaneous intervention. In the disease prone carotid bulb, direct measurement of blood flow characteristics is difficult, and numerical modeling is frequently used to simulate and study the bulb’s unique hemodynamic conditions. When combined with geometry data, numerical modeling can predict the hemodynamics within the bulb utilizing laminar blood flow measurements taken proximal and distal to areas of flow disturbance. However, in order for numerical models to make accurate predictions, input and output boundary conditions must also be accurate.

Using duplex ultrasonography, we obtained multiple measurements of blood velocity profiles from the inflow and outflow segments of in vivo human carotid artery bifurcations. Our findings of skewed velocity profiles at all three locations during both systole and diastole contradict the common assumption that blood velocity profiles away from the bulb are symmetric about the arterial axis. However, our results are in agreement with findings obtained using magnetic resonance imaging of the CCA also describing skewed profiles. We speculate that the observed skewing of the velocity profile in vivo may be due to tortuosity of the artery and cross-sectional asymmetry of the flow lumen. It has been previously reported that even though distal CCA appears to be relatively straight, its curvature is still sufficient for significantly skewing the velocity profile. In particular, it has been suggested that the bend provokes a radial redistribution of momentum to compensate the centrifugal force that, in turn, even in steady flow conditions, yields consistent velocity profile skewing. A detailed investigation of the influence of arterial tortuosity on the velocity profile shape is beyond the scope of the present study. However, the geometries of the arteries in this patient group are being currently analyzed by our team. Preliminary results reveal strong nonplanarity and both in- and out-of-plane curvature of the considered arteries.

It has also been suggested that skewing of the velocity profile may correspond to the presence of secondary flows. From duplex measurements alone it is not possible to infer the value of the secondary velocity components. However, it has been reported that secondary velocities are 10% of the axial velocity in physiologically curved tubes. Such low value therefore indicates that skewing of the velocity profile may be due to presence of the secondary flows, rather than their strength.

Velocity profiles in all arteries were skewed posteriorly both before and after endarterectomy. In the mediolateral direction, the CCA velocity profile is skewed with higher velocities laterally. Similar results for the CCA profile were recently reported. In the ECA, the velocity profile is also skewed laterally, with velocities near the medial wall being higher than those near the lateral wall. The opposite was observed in the ICA, where the velocity profile was skewed medially, but with higher velocities measured near the lateral wall than the medial wall. The finding that velocity profiles tend to be skewed to the inner walls of the bifurcation has been reported previously. However, in these studies, velocity profiles were evaluated close to the bulb and therefore were affected by branching. Our findings demonstrate that profiles do not regain symmetry even after 4 to 5 diameters off the flow divider, where they are usually assumed symmetric. Overall, the shapes of the ve-
The global burden of stroke presents a pressing need for improved understanding of the mechanisms involved in the pathophysiology and treatment of carotid bifurcation disease. Our work demonstrates the importance of considering the entire three-dimensional pulsatile velocity profiles and provides a detailed quantification of the velocity profiles present at the inflow and outflow boundaries of the pre- and postendarterectomy human carotid bifurcation.

The in vivo hemodynamics of these human carotid artery segments are considerably different from those previously generated by in vitro and computer-based models. These detailed in vivo data can be used to design better numerical models that more closely replicate in vivo hemodynamic conditions. These models can help us delineate the association between the complex flow patterns present in the carotid bulb and carotid bifurcation disease, such as atherosclerosis and restenosis, and may also permit in silico development, testing, and optimization of vascular devices to treat disease in the carotid bifurcation.

**AUTHOR CONTRIBUTIONS**

Conception and design: AK, YD, JM, IP  
Analysis and interpretation: AK, YD, JM, IP  
Data collection: AK, IP, AD  
Writing the article: AK, YD, JM, IP  
Statistical analysis: AK  
Critical revision of the article: AK, YD, JM, AD, IP  
Final approval of the article: AK, YD, JM, AD, IP  
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