Impact of blood flow volume in determining the destination of intracardiac thrombi using computational fluid dynamics

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1. Introduction

Cardioembolic stroke due to atrial fibrillation (AF) generally affects the anterior circulation more often than it affects the posterior circulation, while anterior circulation infarction and posterior circulation infarctions show a similar frequency in other stroke subtypes [1]. However, the destination where the thrombi migrate when cardioembolic stroke occurs in each patient remains unclear. Thus, there is notably a certain tendency of intracardiac thrombi to migrate to the anterior cerebral arteries in patients with AF. Therefore, it is worthwhile investigating what influences the distribution of intracardiac thrombi, which arteries are susceptible to occlusion, and why intracardiac thrombi migrate more frequently into the anterior cerebral circulation, to advance our understanding of the pathogenesis of cardioembolic stroke. Computational fluid dynamics (CFD) modeling has attracted increasing attention in cardiocerebrovascular medicine, since it provides detailed blood flow information, reconstructing traditional imaging modalities, including computed tomography (CT) and magnetic resonance imaging (MRI) [2]. CFD analysis helped clarify the movement of intracardiac thrombi by focusing on the blood flow distribution. Herein, we describe a critical case wherein we diagnosed a bilateral internal carotid artery (ICA) territory infarction in a patient with AF who apparently developed nearly simultaneous occlusion in the ICAs bilaterally. A 92-year-old woman with AF who appeared to have developed bilateral occluded common carotid artery (CCA)—ICAs almost simultaneously presented after the sudden onset of coma and quadriplegia and was diagnosed with bilateral ICA territory infarction. The patient died at 4 days after the onset due to the huge infarction. The blood flow in the aorta and the major branches of the aortic arch were examined using computational fluid dynamics (CFD) based on contrast-enhanced computed tomography angiography, which revealed that the right and left CCAs covered larger flow volumes than the other aortic arch branches, suggesting that the intracardiac thrombi migrated into the bilateral CCA—ICAs in the patient. The study findings imply that the fluid dynamic factors of major branches from the aortic arch can be one of the decisive factors for intracardiac thrombus distribution. CFD could simulate patient-specific hemodynamics and may be useful to investigate the susceptibility of the aortic arch branches to occlusion by AF-induced intracardiac emboli.

2. Case presentation

A 92-year-old woman presented at our emergency room under ambulatory care after a sudden onset of coma and quadriplegia. The patient had past medical histories of asymptomatic myocardial ischemia, chronic heart failure, and persistent AF but received no anticoagulant medication. Her blood pressure was 205/102 mmHg, and she had an irregular heart rate of 79 bpm, with 95% oxygen saturation on room air. A neurological examination showed a normal pupil size (3 mm/3 mm), bilateral positive pupillary light reflex, roving eye movement, positive oculocephalic reflex, decorticate posture with a Glasgow
Fig. 1. Magnetic resonance imaging (MRI) and contrast-enhanced computed tomography (CT) of the brain on admission.
(A-C) The diffusion-weighted MRI (A), apparent diffusion coefficient map (B), and fluid-attenuated inversion recovery MRI (C) showing acute bilateral internal carotid artery (ICA) territory infarction, (D) T2*-weighted MRI showing the susceptibility vessel sign (arrows) in the internal carotid artery and middle cerebral artery bilaterally; (E) MR angiography showing the lack of signals in the intracranial ICA, middle cerebral artery, and anterior cerebral artery; (F) Contrast-enhanced CT showing the contrast deficit in the left atrial appendage (arrowhead).
Abbreviation: R, right; L, left.
Coma Scale score of 5, and a National Institutes of Health Stroke Scale score of 34. On brain non-contrast MRI, diffusion-weighted MRI (Fig. 1A) and apparent diffusion coefficient map (Fig. 1B) showed almost the same signal intensity in the infarcted lesions of the right and left ICA territories, and fluid-attenuated inversion recovery revealed no such lesions with a high signal intensity (Fig. 1C), illustrating acute cerebral infarction in the bilateral ICA territories with a nearly simultaneous onset. T2*-weighted imaging showed the susceptibility vessel sign in the bilateral distal ICAs to the middle cerebral artery (MCA) (Fig. 1D). The ICA, MCA, and anterior cerebral arteries were not visible bilaterally upon brain MR angiography (MRA), suggesting bilateral CCA or proximal ICA occlusion (Fig. 1E), whereas the electrocardiogram showed AF. Contrast-enhanced CT demonstrated a contrast deficit in the left atrial appendage (LAA) (Fig. 1F). Based on these clinical findings, the patient was diagnosed with cardioembolic bilateral ICA occlusion and acute cardioembolic stroke due to AF. Any reperfusion therapies, such as recombinant tissue plasminogen activator administration, mechanical thrombectomy, or other antithrombotic treatments, were not performed considering the massive infarctions. Eventually, the patient died on day 4 after the stroke onset.

An autopsy was performed after the bereaved family provided written informed consent. The autopsy revealed bilateral CCA–ICA occlusion with red fibrin thrombi, which were also detected in the LAA, with severe ischemic changes with softening in the whole brain and herniation. These pathological findings suggested that the AF-associated fibrin thrombi in the LAA moved to the bilateral CCA–ICAs and induced sudden occlusion of the CCA–ICAs and subsequent cardioembolic stroke.

To clarify the mechanism of embolic bilateral CCA–ICA occlusion, we created a geometrical model of the thoracic aorta and its branches from contrast-enhanced CT angiography (CTA) images and analyzed the blood flow dynamics in three different situations using CFD (Fig. 2). The Navier-Stokes’ equations of blood flow in a three-dimensional (3D) domain were numerically coupled to the peripheral blood flow models in a 0D domain [3]. The flow volume (mL/min) and branch-wise proportions of the flow volume in each branch from the aortic arch were examined under the following three scenarios: 1) all vessels were open; 2) the right CCA was first occluded; and 3) the left CCA was first occluded in the lower images.

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**Fig. 2.** Schematic representation of blood flow simulation procedure.

**Fig. 3.** Streamlines color-coded with velocity magnitude. The upper figure showing the name of each artery. (A) Right subclavian artery, (B) Right common carotid artery, (C) Right vertebral artery, (D) Left common carotid artery, (E) Left vertebral artery, (F) Left subclavian artery. Numbers represent the flow rates at the aortic branches (mL/min) when 1) all vessels were open; 2) the right CCA was first occluded; and 3) the left CCA was first occluded in the lower images.
(as premorbid state); 2) the right CCA was first occluded; and 3) the left CCA was first occluded, as simulated previously [4]. Occlusion of the unilateral CCA was simulated separately because the thrombi do not always move to both the CCAs simultaneously. The results demonstrated that in situation (1), blood flow to the right CCA was 516 mL/min (10.4% of the total) and that to the left CCA was 392 mL/min (7.9%), which were greater than the blood flow to the other branches. Additionally, blood flow to the contralateral open CCA was higher in situations (2) and (3) than that in situation (1), with the greatest flow volume among the branches (Fig. 3).

3. Discussion

The causes of the varied locations of thromboembolism in the course of AF remain to be elucidated. The anatomical distribution of thrombi may be generally influenced by arterial branching and the course of blood flow [5]. The results of our CFD analysis suggested that the intracardiac thrombi were prone to migrating into arteries, which were characterized by high-volume blood flow. This report may indicate a plausible explanation of why a cardioembolic stroke affects the anterior circulation more often than it affects the posterior circulation [1]. Thus, CFD modeling displays blood flow distribution that varies by blood-vessel geometry and provides novel insights into cardioembolic stroke characteristics. Thereby, CFD modeling can assess blood flow dynamics even in case with different arterial geometries such as those with arterial occlusion (e.g., unilateral ICA or CCA occlusion) and arterial stenosis. To gain novel insights into cerebral and systemic embolic events due to AF, the blood flow volume assessed by CFD can be useful to identify the risk of an embolic event.

We occasionally encounter problems in determining whether the case of arterial occlusion is acute or chronic. The dynamics of blood flow around the occluded arteries should be different between acute and chronic occlusion, and flow volume/velocity and wall shear stress assessed by CFD might be different between the two groups. Therefore, CFD could play an important role for investigating the mechanisms of atherothrombotic stroke with gradual stenosis/occlusion as well as cardioembolic stroke induced by sudden arterial occlusion.

4. Conclusions

We report a rare case of bilateral ICA territory infarctions due to occlusion of both CCA-ICAs in a patient with AF. The in silico CFD model successfully estimated the blood flow volume in the branches from the aortic arch and predicted the destination of intracardiac thrombi, which migrated to the branches receiving a larger blood flow. Our study findings imply that CFD modeling plays a pivotal role to look beyond the pathogenesis of cardioembolic stroke.

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**Author contributions**

YH and NT managed the patients and collected the data. YH, MN, and MI wrote/edited the manuscript. MN conducted the CFD analysis, and analyzed the obtained data.

**CRediT authorship contribution statement**

Yorito Hattori: Conceptualization, Methodology, Visualization, Writing - original draft, Writing - review & editing. Naoki Tagawa: Investigation. Masanori Nakamura: Software, Writing – review & editing, Visualization. Masafumi Ihara: Writing – review & editing, Supervision.

**Declaration of Competing Interest**

None.

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