Association of Embolic Stroke Territory with Aortic Arch Retrograde Flow in patients with Cryptogenic Stroke

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Introduction: Cryptogenic stroke is a nonlacunar ischemic stroke of unknown but presumably embolic etiology despite an exhaustive search for etiologic causes[1], accounting for 20-25% of all embolic strokes in the US [2-4]. Plaques of the aorta have been implicated as causes of embolic stroke for several decades [1]. It is well understood that complex plaques with a maximum thickness ≥4 mm or those with mobile surface thrombi constitute high-risk sources for antegrade thromboembolic events. However, it is unclear to what extent plaques of the descending aorta predispose to embolic stroke due to retrograde diastolic blood flow that connecting the embolic source (plaque in the descending aorta) with the vessels perfusing the brain. The potential causative role of descending aortic plaques as a source of embolic stroke was recently demonstrated in acute stroke patients [4]. Retrograde embolization was detected in more than 55% of patients, representing a new mechanism for embolic stroke to all cerebral vascular territories [4]. Importantly, this mechanism constituted the only probable source of retinal or cerebral infarction in 24% of patients with cryptogenic stroke [5]. The purpose of this prospective study was to further evaluate the presence of retrograde diastolic flow from the descending thoracic aorta (DAo) into the great vessels as a potential pathogenic mechanism for cryptogenic atheroembolic stroke. We hypothesize that left hemispheric territory stroke will be more common in patients with cryptogenic stroke and that retrograde flow pathways assessed using 4D flow MRI will correlate with stroke territory as determined on diffusion weighted MRI.

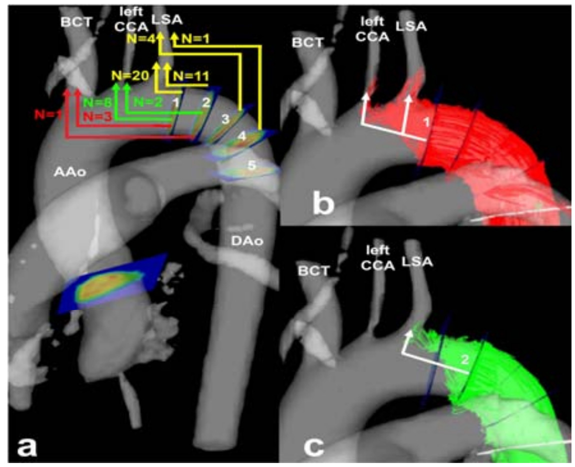

Figure 1: Using 4D flow MRI for visualization of retrograde flow from the descending thoracic aorta into the aortic arch. **A-** Summary of maximal retrograde diastolic flow distance from each of the five planes positioned in the Aortic Arch and Descending Aorta from the origin of the Left Subclavian Artery. Each plane is separated by 10mm. red=InA, green=LCCA, yellow=LSA. **B-** 3D streamlines visualization of a 53 year old stroke patient throughout the cardiac cycle emitting from the first plane with regurgitant flow into the LCCA and LSA.**C-** Same patient as above but with the regurgitant flow emitted from the second plane. (InA = innominate artery; LCCA= left common carotid artery; LSA = Left subclavian artery.

Materials and Methods: 4D flow MRI was performed at 1.5T or 3T (MAGNETOM Aera, Avanto, or Skyra, Siemens Medical Systems, Erlangen, Germany) in 35 patients (17 men, 63±17 years) with cryptogenic stroke. Aortic blood flow was measured using ECG and respiration synchronized 4D flow MRI (3-directional venc=150cm/s, spatial res 2.0-2.8mm^3, temp res 40-44 msec) with full 3D coverage of the entire thoracic aorta [5]. The extent of retrograde flow originating in the descending aorta (DAo) was evaluated using 3D blood flow visualization (EnSight, CEI, Apex, NC). To measure the maximum distance of diastolic retrograde flow in the DAo, a series of 5 emitter planes were positioned at 10 mm intervals from the left subclavian artery origin and 3D pathlines were displayed to depict blood flow direction and pattern (Figure 1). Embolization pathways from the DAo were considered present if retrograde flow extended to a great vessel origin. Stroke location was determined on diffusion weighted MRI and correlated with 4D flow MRI findings. Differences in the prevalence of left- and right-sided strokes were compared in patients with and without retrograde flow using the chi-squared test; p-values of < 0.05 were considered significant.

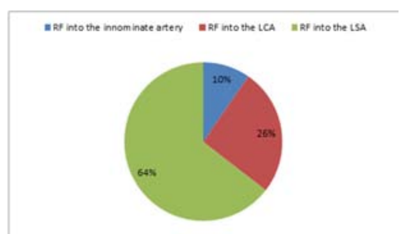

Figure 2: Graphical breakdown of retrograde diastolic flow into the great vessel origins in the 20 subjects demonstrating retrograde diastolic flow at 4D flow MRI. There is decreasing prevalence of retrograde flow into the great vessel origins with increasing distance from the descending thoracic aorta.

Results: 4D flow MRI enabled blood flow visualization in the thoracic aorta of all patients. Diastolic retrograde flow was observed in 20 patients (57%), visualized from the DAo into the innominate artery (InA) in 3 subjects (8.57%), into the left common carotid artery (LCCA) in 8 (23.6%), and into the left subclavian artery (LSA) in 20 patients (57%) (Figure 2). Retrograde flow originated from DAo locations as far as 30mm distal to the left subclavian artery (plane 4) as summarized in figure 1. There was 80% concordance (16 of 20) with stroke location on imaging with retrograde diastolic flow visualized into the feeding vessels of the affected cerebral area. Left-sided hemispheric strokes/transient ischemic attacks were similarly prevalent in patients with and without retrograde flow (65%, 13 of 20 vs 66%, 10 of 15) (p=0.192)

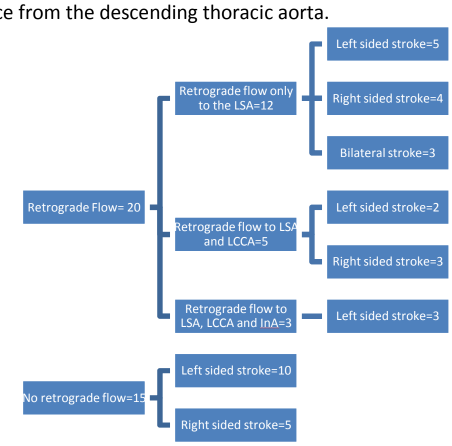

Figure 3: Hemispheric distribution of stroke depending on retrograde flow.

Discussion: Our initial results demonstrate that retrograde diastolic flow visualized at 4D flow MRI from the descending thoracic aorta reaches the great vessel origins, confirming a potential etiology for cryptogenic atheroembolic stroke. A larger cohort is needed to validate these results, matching cryptogenic stroke distribution in the context of patient specific variations in cerebral vascular anatomy with the prevalence of retrograde flow into the great vessel origins.

References:

1.Liberman, A.L. and S. Prabhakaran, *Cryptogenic stroke: how to define it? How to treat it?* Curr Cardiol Rep, 2013. 15(12): p. 423.***2.***Amarenco, P., et al., *Aortic arch atheroma and the risk of stroke.* Curr Atheroscler Rep, 2006. 8(4): p. 343-6. ***3.***Feigin, V.L., et al., *Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century.* Lancet Neurol, 2003. 2(1): p. 43-53.***4.***Guercini, F., et al., *Cryptogenic stroke: time to determine aetiology.* J Thromb Haemost, 2008. 6(4): p. 549-54.***5.***Markl, M., et al., *4D flow MRI.* J Magn Reson Imaging, 2012. **36**(5): p. 1015-36.