Left Atrial Appendage Morphology and Embolic Stroke of Undetermined Source: A Cross-Sectional Multicenter Pilot Study

Shadi Yaghi, MD,* Andrew D. Chang, MS,* Peter Hung, BS,† Brian Mac Grory, MD,‡ Scott Collins, PhD,§ Ajay Gupta, MD,‖ Jacques Reynolds, DO,* Caitlin B. Finn, BS,† Morgan Hemendinger, BS,* Shawna M. Cutting, MD,* Ryan A. McTaggart, MD,§ Mahesh Jayaraman, MD,*,§,¶ Audrey Leasure, BS,‡ Lauren Sansing, MD,‡ Nikhil Panda, MD,# Christopher Song, MD,# Antony Chu, MD,# Alexander Merkler, MD,† Gino Gialdini, MD,† Kevin N. Sheth, MD,‡ Hooman Kamel, MD,† Mitchell S.V. Elkind, MS,**,†† David Greer, MD,‡‡ Karen Furie, MD MPH,* and Michael Atalay, MD, PhD§

Background: The left atrial appendage (LAA) is the main source of thrombus in atrial fibrillation, and there is an association between non-chicken wing (NCW) LAA morphology and stroke. We hypothesized that the prevalence of NCW LAA morphology would be higher among patients with cardioembolic (CE) stroke and embolic stroke of undetermined source (ESUS) than among those with noncardioembolic stroke (NCS). *Methods:* This multicenter retrospective pilot study included consecutive patients with ischemic stroke from 3 comprehensive stroke centers who previously underwent a qualifying chest computed tomography (CT) to assess LAA morphology. Patients underwent inpatient diagnostic evaluation for ischemic stroke, and stroke subtype was determined based on ESUS criteria. LAA morphology was determined using clinically performed contrast enhanced thin-slice chest CT by investigators blinded to stroke subtype. The primary predictor was NCW LAA morphology and the outcome was stroke subtype (CE, ESUS, NCS). *Results:* We identified 172 patients with ischemic stroke who had a clinical chest CT performed. Mean age was 70.1 ± 14.3 years and 51.7% were male. Compared with patients with NCS, the prevalence of NCW LAA morphology was higher in patients with CE stroke (58.7% versus 46.3%, $P = .1$) and ESUS (58.8%

From the *Department of Neurology, The Warren Alpert Medical School of Brown University, Providence, Rhode Island; †Departments of Neurology and Feil Family Brain and Mind Research Institute, Weill Cornell Medical College, New York, New York; ‡Department of Neurology, Yale University Medical Center, New Haven, Connecticut; §Department of Diagnostic Imaging, The Warren Alpert Medical School of Brown University, Providence, Rhode Island; ‖Department of Radiology, Weill Cornell Medical College, New York, New York; ¶Department of Neurosurgery, The Warren Alpert Medical School of Brown University, Providence Rhode Island; #Department of Internal Medicine, Division of Cardiology, The Warren Alpert Medical School of Brown University, Providence, Rhode Island; **Department of Neurology, College of Physicians and Surgeons; ††Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York; and ‡‡Departments of Neurology, Boston University Medical Center, Boston, Massachusetts.

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Address correspondence to Shadi Yaghi, MD, The Warren Alpert Medical School of Brown University, 353 Eddy Street APC 530, Providence, RI 02903. E-mail: shadiyaghi@yahoo.com.

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versus 46.3%, $P = .2$), but this difference did not achieve statistical significance. *Conclusion:* The prevalence of NCW LAA morphology may be similar in patients with ESUS and CE, and may be higher than that in those with NCS. Larger studies are needed to confirm these associations. **Key Words:** Cryptogenic stroke—embolic stroke of undetermined source—left atrial appendage—morphology—ischemic stroke—atrial fibrillation—atrial cardiopathy.
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Introduction

Embolic stroke of undetermined source (ESUS) accounts for 20%-30% of ischemic strokes. Atrial dysfunction or "cardiopathy" diagnosed through serum, electrocardiographic, and echocardiographic biomarkers has been recently introduced as a potential mechanism of embolism in ESUS.[1,2]

Although the left atrial appendage (LAA) is the site of the majority of cardiac emboli in patients with atrial fibrillation (AF), there are very limited data on whether it is also a source of thrombus in patients with ESUS. The LAA morphology has been categorized into 4 different morphologies: chicken wing (48%), cactus (30%), windsock (19%), and cauliflower (3%).[3] Although LAA volume may change over time, the LAA morphology is thought to remain unchanged. In patients with AF, studies have shown an association between a non-chicken wing (NCW) morphology and ischemic stroke risk.[3,4] We hypothesized that the prevalence of NCW LAA morphology is similar in patients with cardioembolic (CE) stroke and ESUS and different from those in patients with established noncardioembolic mechanisms.

Methods

Patient Population

We performed a multicenter retrospective study of consecutive patients with ischemic stroke from 3 institutions (Rhode Island Hospital [n = 39 patients between April 1, 2015 and July 31, 2015], Cornell University Medical Center [n = 107 patients between January 1, 2011 until December 31, 2015], and Yale University Medical Center [n = 26 patients between July 1, 2014 and September 16, 2016]). Patients underwent standard inpatient diagnostic evaluation for ischemic stroke according to local practice, and stroke subtype was determined based on ESUS criteria.[5]

Consecutive patients identified in prospective ischemic stroke databases at each site were cross-matched with the picture archiving and communication system (PACS) database to identify those patients with one or more qualifying chest computed tomography (CT) scans before the data collection date. Qualifying chest CTs (not part of the diagnostic evaluation of ischemic stroke) were ones using the technique described below. We included all patients 18 years or older admitted with a diagnosis of ischemic stroke during the study period who underwent a qualifying chest CT for review on or before the admission date. Institutional review boards in each site approved the study and waived the need for consent.

Chest CT with Contrast Protocol

All CT studies were conducted on either a 64-row CT scanner (LightSpeed VCT, General Electric Healthcare) or a 16-row CT scanner (Sensation 16; Siemens Medical Solutions). In general, qualifying studies were obtained using protocols that included thin-slice reconstruction (≤2.5 mm) with submillimeter in-plane resolution and rapid (>3 cc/s) intravenous administration of iodinated contrast material (≥80 cc). Patients were scanned supine with a scan range based on the scout view from 1 cm below the lowest costophrenic angle to 1 cm above the lung apex. Thin axial slice datasets were transferred to PACS along with coronal plane reconstructions.

LAA Morphology and Analysis

Before LAA morphological analysis, thin-slice image data were retrieved from PACS and imported into a thin-client server where detailed multiplanar and volumetric reconstruction could be performed using commercially available software (iNtuition, TeraRecon).

During initial postprocessing, the LAA was selected out using so-called cut-plane viewing to remove surrounding structures. Volume rendering then permitted unobstructed viewing from any rotational perspective. Image processing was performed under the supervision of an experienced radiology technologist (S.C.) in the 3-dimensional imaging laboratory at Rhode Island Hospital. Images were stored on the thin-client server and were available for the readers (blinded to the clinical data and stroke subtype) to review. The LAA morphology was determined, based on criteria used in prior studies,[3] independently by 2 different readers with excellent inter-reader reliability (kappa = .9) and blinded to subject and stroke subtype.

Primary Predictor and Covariates

The primary predictor was NCW LAA morphology, and covariates included age, sex, history of hypertension, history of hyperlipidemia, history of diabetes, history of prior stroke, history of coronary heart disease, history of

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