Characteristics of Anatomy and Function of the Left Atrial Appendage and Their Relationships in Patients with Cardioembolic Stroke: A 3-Dimensional Transesophageal Echocardiography Study

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Background: Increasing attention is being paid to the left atrial appendage (LAA) in the context of risk stratification in cardioembolic stroke (CES) and the requirement for meticulous planning of percutaneous closure device implantation. However, detailed systematic assessment of the LAA remains limited. *Methods:* This study evaluated the anatomy and function of LAA using 3-dimensional transesophageal echocardiography (3D-TEE) on 194 consecutive patients older than 50 years old hospitalized exclusively for CES. Patients were stratified into 3 groups on the basis of cardiac rhythm: (1) chronic atrial fibrillation (AF), n = 53; (2) paroxysmal AF, n = 26; and (3) no detected AF, n = 115. *Results:* Significant differences between the groups were observed for anatomical (orifice area [OA], depth, diastolic volume) and functional parameters (ejection fraction [EF], flow velocity [FV]), as measured by 3D-TEE. The anatomical parameters were consistently the greatest, and functional parameters were the poorest, in the group with chronic AF. There were significant inverse correlations between them (r = –.33, $P = .0003$ for depth and EF; r = –.27, $P = .0020$ for depth and FV; r = –.22, $P = .016$ for OA and EF; and r = –.38, $P < .0001$ for OA and FV). *Conclusions:* LAA morphology and function were strongly affected by cardiac rhythm disturbances. Patients with chronic AF had the greatest LAA dimensions, areas, and volumes as well as the lowest LAA functions. An inverse correlation was observed between LAA size and function. **Key Words:** Left atrial appendage—embolic stroke—transesophageal echocardiography—atrial fibrillation.

Introduction

Cardioembolic stroke (CES) accounts for 14%-30% of all strokes and tends to result in large infarcts and often in death or severe functional disorders. It is well-known that atrial fibrillation (AF) is the most common cause of CES. Relative to patients without AF, the risk of stroke is estimated at up to 5 times higher than in those with AF. Because the prevalence of AF increases with patient age, the risk of CES also becomes greater as the population ages.[1,2]

Generally, by summing clinical risk factors, CHADS2 and CHA2DS2-VASc scores determine the risk of cerebral infarction in patients with AF quite well.[3,4] In addition to these clinical determinants, imaging findings may impact

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on the prediction of CES, including spontaneous echo contrast imaging of the left atrium (LA) and detecting thrombi in the left atrial appendage (LAA) using transesophageal echocardiography (TEE).[5] Very importantly, 90% of thrombi in patients with AF are located in the LAA, and there is a negative correlation between LAA flow velocity and prevalence of thrombus formation in the LAA.[6-10] Accordingly, some anatomical or functional parameters of the LAA could potentially be applied for predicting onset of cerebral infarction, and could possess even higher diagnostic value than CHADS2 and CHA2DS2-VASc scoring.

Furthermore, recently, instead of systemic anticoagulant therapy, a new strategic option, catheter-based LAA occlusion, has become popular for preventing cerebral infarction. This technique demands precise detailed understanding of the LAA.[11,12] In general, 3-dimensional (3D) examination must be applied for this purpose, and TEE allows both anatomical and functional investigations of LAA in a convenient manner. However, such investigations still remain few and far between, although several previous studies using 3D-TEE targeted the whole group of patients with AF.[13-16] Nonetheless, investigations exclusively of patients who had actually had CES are required to better discriminate the risk of cerebral infarction. Accordingly, we planned a retrospective study to investigate (1) the characteristic anatomy and function of LAA and (2) the relationships between anatomical parameters and functional parameters in patients who had actually had a CES.

Methods

Study Population

Patients who had CES and had undergone 3D-TEE to locate residual thrombus and cardiac abnormalities in Iwate Medical University hospital were retrospectively surveyed from September 2011 to March 2015. This study investigated anatomical and functional features of LAA of transthoracic echocardiography (TTE) and TEE in this cohort. Diagnosis of CES was made by concordant views of several neurology experts, based on comprehensive judgment of imaging (carotid artery echo, brain computed tomography and/or magnetic resonance imaging) and physical examination, and stroke subtype was determined according to the Trial of Org 10172 in Acute Stroke Treatment stroke classification.[17]

Exclusion criteria were (1) patients diagnosed as atherothrombotic or having lacunar infarction; (2) patients younger than 50 years old, because of relatively higher prevalence of the other etiologies of stroke, such as paradoxical embolization,[18] Trousseau syndrome,[19] and vertebral artery dissection[20]; and (3) patients with significant valvular heart disease, because these disorders significantly affect the anatomy and function of LA and LAA. Accordingly, a total of 194 consecutive patients, classified as having “cardioembolism” according to Trial of Org 10172 in Acute Stroke Treatment criteria, were enrolled in this study.

Echocardiographic Studies

All patients received both TTE and 3D-TEE. TTE images were acquired using a commercially available ultrasound imaging system (EUB-8500: HITACHI, ProSound α-10: HITACHI-ALOKA, IE33: Philips). Both parasternal and apical views of TTE were assessed. Standard echocardiogram parameters were measured by experienced sonographers, including left ventricular ejection fraction (LVEF), left atrial diameter (LAD), left ventricular end-diastolic diameter and volume, left ventricular end-systolic diameter (LVESD) and volume, left ventricular mass index, left atrial volume index (LAVI), deceleration time, and E/e′. LVESD and left ventricular end-diastolic diameter were measured on an M-mode image or a 2-dimensional (2D) image derived from an LV long-axis view at the parasternal level. Representative LV volumetric parameters, left ventricular end-diastolic volume, left ventricular end-systolic volume, and the LVEF were measured using a modified Simpson’s method. In addition, in terms of quantification of LA parameters, end-systolic and end-diastolic LA volumes were measured using a modified Simpson’s method in the apical 4- and 2-chamber views.

3D-TEE was performed using an ultrasound imaging system with a 3D matrix-array transesophageal 7-15 Hz transducer (X7-2) (iE33, Philips Medical Systems, Andover, MA). All 2D and 3D-TTE measurements were determined based on the recommendations of the American Society of Echocardiography.[21] LAA flow velocities by pulsed-Doppler were measured as LAA emptying and filling flow velocities at multiplane angles of 90 degrees as the average of 3 consecutive cardiac cycles in patients with normal sinus rhythm, and 5 consecutive cardiac cycles in patients with AF. Quantitative assessments of LAA parameters were performed with QLAB GI-3DQ software (Philips Medical Systems). All contours for measurements were manually traced by expert physicians (T.A., K.A., M.S.). Traced contours were also evaluated by independent expert echocardiologists (T.A., M.Y.) to confirm their accuracy and finally validated at least twice by other investigators.

Figure 1 illustrates definitions of measurements of the LAA of TEE images. For 2D-TEE analyses, long- and short-axis diameters at orifice, orifice area, and depth were measured. LAA long-axis views were obtained at a level including the mitral valve annulus, and the lateral ridge of the left superior pulmonary vein and LAA orifice area was determined.[22] The symmetry index of the orifice was defined as the short-axis diameter divided by the long-axis diameter at the LAA orifice. Terminology used to describe the cardiac cycle may be confused between atrium and ventricle. For example, atrial “systole” corresponds