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Atrial Fibrillation

Does the Left Atrial Appendage Morphology Correlate With the Risk of Stroke in Patients With Atrial Fibrillation?

Results From a Multicenter Study

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Objectives This study investigated the left atrial appendage (LAA) by computed tomography (CT) and magnetic resonance imaging (MRI) to categorize different LAA morphologies and to correlate the morphology with the history of stroke/transient ischemic attack (TIA).

Background LAA represents one of the major sources of cardiac thrombus formation responsible for TIA/stroke in patients with atrial fibrillation (AF).

Methods We studied 932 patients with drug-refractory AF who were planning to undergo catheter ablation. All patients underwent cardiac CT or MRI of the LAA and were screened for history of TIA/stroke. Four different morphologies were used to categorize LAA: Cactus, Chicken Wing, Windsock, and Cauliflower.

Results CT scans of 499 patients and MRI scans of 433 patients were analyzed (age 59 ± 10 years, 79% were male, and 14% had $CHADS_2$ [Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack] score ≥2). The distribution of different LAA morphologies was Cactus (278 [30%]), Chicken Wing (451 [48%]), Windsock (179 [19%]), and Cauliflower (24 [3%]). Of the 932 patients, 78 (8%) had a history of ischemic stroke or TIA. The prevalence of pre-procedure stroke/TIA in Cactus, Chicken Wing, Windsock, and Cauliflower morphologies was 12%, 4%, 10%, and 18%, respectively ($p = 0.003$). After controlling for $CHADS_2$ score, gender, and AF types in a multivariable logistic model, Chicken Wing morphology was found to be 79% less likely to have a stroke/TIA history (odd ratio: 0.21, 95% confidence interval: 0.05 to 0.91, $p = 0.036$). In a separate multivariate model, we entered Chicken Wing as the reference group and assessed the likelihood of stroke in other groups in relation to reference. Compared with Chicken Wing, Cactus was 4.08 times ($p = 0.046$), Windsock was 4.5 times ($p = 0.038$), and Cauliflower was 8.0 times ($p = 0.056$) more likely to have had a stroke/TIA.

Conclusions Patients with Chicken Wing LAA morphology are less likely to have an embolic event even after controlling for comorbidities and $CHADS_2$ score. If confirmed, these results could have a relevant impact on the anticoagulation management of patients with a low-intermediate risk for stroke/TIA. (J Am Coll Cardiol 2012;60:531–8)
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The left atrial appendage (LAA) represents one of the major sources of cardiac thrombus formation responsible for transient ischemic attack (TIA)/stroke in patients with atrial fibrillation (AF) (1–3). Its anatomic structure is challenging

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Abbreviations and Acronyms

AF = atrial fibrillation

$CHADS_2$ = Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack

CHA_2DS_2-VaSc = Congestive heart failure, Hypertension, Age (>75 = 2 points, 65 to 74 = 1 point, <65 = 0 point, Diabetes mellitus, prior Stroke or transient ischemic attack, female gender

CI = confidence interval

CT = computed tomography

LA = left atrium

LAA = left atrial appendage

MRA = magnetic resonance angiography

MRI = magnetic resonance imaging

OR = odds ratio

3D = 3-dimensional

TIA = transient ischemic attack

(3). Embriologically it is a remnant of the primordial left atrium (LA). The LAA lies anteriorly in the atrioventricular sulcus in close proximity to the left circumflex artery, the left phrenic nerve, and the left pulmonary veins (3–5).

The shape of the LAA is variable. Several studies have described the LAA as a long tubular and hooked structure with different lobes. The imaging of the different structures and lobes is of utmost importance to diagnose the presence of LAA thrombus, especially in patients with nonvalvular AF (3,6–8).

The widespread use of LA ablation procedures and the presence of an LAA occlusion device for the treatment of patients with AF has increased the interest for this structure (9–11). Multidetector computed tomography (CT) and magnetic resonance imaging (MRI) are well-known imaging techniques that are able to detect high-quality images of the LAA (12,13).

We studied the LAA by CT and MRI to categorize different LAA morphologies and tried to correlate the different morphologies with the patient history of stroke/TIA.

Methods

Patient population. The study population consisted of 932 consecutive patients with drug-refractory AF planning to undergo transcatheter AF ablation, in whom pre-ablation cardiac CT or MRI was performed. Care was taken to obtain LAA frames in all patients. The $CHADS_2$ (Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack) score of each patient was calculated before the occurrence of any thromboembolic event. History of stroke/TIA was collected using patients' chart reviews. LAAs were categorized into 4 different morphologies by CT scan and MRI: Cactus, Chicken Wing, Windsock, and Cauliflower (as discussed later) (Table 1, Figs. 1 to 4).

Computed tomography. Cardiac CT imaging of the LAA was performed as previously described with a 64-channel cardiac CT angiography (LightSpeed VCT, GE Healthcare, Alexandria, Virginia) (3). Briefly, patients were scanned with contrast-enhanced electrocardiogram-gated CT scan (LightSpeed Ultra, GE Healthcare). The slice acquisition thickness ranged from 0.625 to 1.25 mm. Three-dimensional (3D) structures of the LA and LAA were constructed using the volume-rendered postprocessing technique. Standard measurements of LAA volume, velocity, and diameters were obtained. The morphol-

Table 1 Baseline Characteristics

	Overall Population (n = 932)	Type 1 (Cactus) (n = 278)	Type 2 (Chicken Wing) (n = 451)	Type 3 (Windsock) (n = 179)	Type 4 (Cauliflower) (n = 24)	p Value	Groups With Pairwise Significant Difference
Age, yrs	59 ± 10	59 ± 09	57 ± 11	59 ± 10	62 ± 15	0.097	
Male	734 (79%)	218 (78%)	356 (79%)	147 (82%)	13 (55%)	0.019	4 vs. 3; 4 vs. 2
AF type							
Paroxysmal	548 (59%)	167 (60%)	266 (59%)	100 (56%)	15 (64%)	0.810	
Persistent	336 (36%)	89 (32%)	167 (37%)	73 (41%)	7 (28%)	0.235	
Long-standing persistent	48 (5%)	22 (8%)	18 (4%)	6 (3%)	2 (8%)	0.086	
AF duration, months	46 (12–83)	48 (14–86)	46 (12–84)	38 (10–82)	44 (8–88)	0.404	
BMI	27 ± 04	27 ± 04	27 ± 04	27 ± 03	26 ± 03	0.906	
Dyslipidemia	218 (23%)	68 (25%)	99 (22%)	47 (27%)	4 (18%)	0.565	
Hypertension	450 (48%)	143 (52%)	201 (45%)	95 (53%)	11 (45%)	0.150	
CHF	42 (5%)	9 (3%)	19 (4%)	13 (7%)	1 (4%)	0.212	
Diabetes	40 (4%)	19 (7%)	13 (3%)	6 (4%)	2 (9%)	0.547	
Prior stroke/TIA	78 (8%)	35 (12%)	20 (4%)	19 (10%)	4 (18%)	<0.001	2 vs. 1; 2 vs. 3
CAD	45 (5%)	15 (5%)	24 (5%)	4 (2%)	2 (9%)	0.643	
$CHADS_2$ 0*	428 (46%)	115 (42%)	237 (53%)	67 (37%)	8 (33%)	<0.001	2 vs. 3; 2 vs. 1
$CHADS_2$ 1*	377 (40%)	111 (40%)	173 (38%)	84 (47%)	9 (36%)	0.258	
$CHADS_2$ ≥2*	127 (14%)	52 (19%)	41 (9%)	28 (16%)	7 (27%)	<0.001	2 vs. 1; 2 vs. 4
LVEF, %	60 ± 07	60 ± 08	59 ± 07	60 ± 07	60 ± 02	0.895	
LAA volume	14.26 ± 06.17	14.63 ± 07.58	13.82 ± 05.3	14.98 ± 06.71	12.71 ± 03.8	0.781	
LAA velocity, mm	74.54 ± 25.43	69.45 ± 28.43	77.34 ± 26.34	79.04 ± 29.84	78.00 ± 18.39	0.257	

Values are mean ± SD, n (%), or median (interquartile range). *The reported $CHADS_2$ scores have been calculated before any thromboembolic event.

AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; $CHADS_2$ = Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack; CHF = congestive heart failure; IQR = interquartile range; LAA = left atrial appendage; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

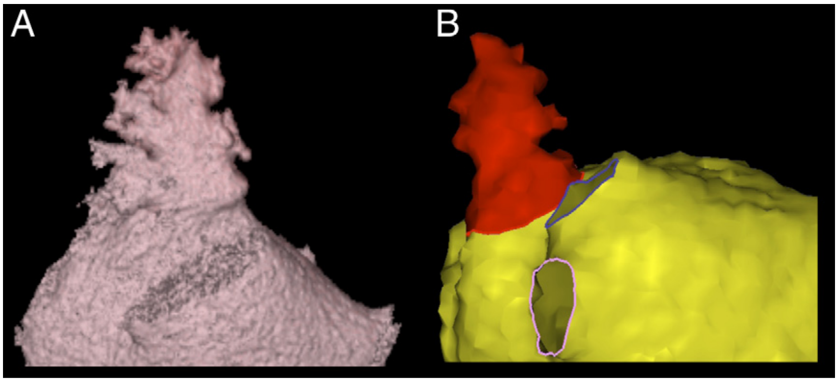

Figure 1 **CT and MRI Scans of a Cactus LAA Morphology**

The Cactus LAA morphology presents a dominant central lobe with secondary lobes extending from the central lobe in both superior and inferior directions. CT **(A)** and MRI **(B)**. CT = computed tomography; LAA = left atrial appendage; MRI = magnetic resonance imaging.

ogy of the LAA was also evaluated using multiplanar reconstruction. LAA morphologies were classified by 2 expert cardiac CT radiologists, who were blinded to the clinical data and history of stroke/TIA.

Magnetic resonance imaging. Contrast-enhanced MRI of the LA was performed by intravenous administration of 0.2 mmol/kg of contrast agent (Gadobutrol, GADOVIST, Bayer S.P.A., Berlin, Germany), followed by a bolus of 20 ml of physiological solution. Images were obtained with a body-array coil 1.5-T MRI system (Magneton Avanto 1.5-T, Siemens, Erlangen, Germany). 3D magnetic resonance angiography (MRA) was obtained with a breath-hold 3D fast-field spoiled gradient echo imaging sequence performed in sagittal, coronal, and axial views to obtain an anatomic view of the entire thorax. A narrow bandwidth of 31.25 kHz was used to reduce noise and improve the signal-to-noise ratio. The fractional echoes (echo time of 1.08 ms) were used to provide T1-weighting and minimize flow artifacts, and a flip angle of 20 degrees was chosen to enhance background suppression. By these settings, contrast-enhanced MRA achieves high spatial resolution (between 0.8 mm and 1.5 mm). The final 3D volume was acquired as a coronal slab (typical field of view 40 cm, range 36 to 44 cm), using a rectangular field-of-view to decrease the acquisition time of the sequence. Temporal resolution was committed to the bolus tracking technique (CARE Bolus, Siemens AG, Malvern, Pennsylvania) guaranteeing the highest LA signal intensity by starting a multiphase spoiled gradient echo image series in a coronal view at the exact time during which the bolus passed through the left ventricle–aortic root. To keep speed magnetization in steady state during the acquisition (repetition time 2.84 ms), contrast-enhanced MRA measurements were not electrocardiogram gated. Another reason not to use gating was that the entire measurement time had to be minimized to follow the bolus of the contrast agent. Motion artifacts from breathing were eliminated by patient's breath-hold for the time of the sequence ($<$15 s).

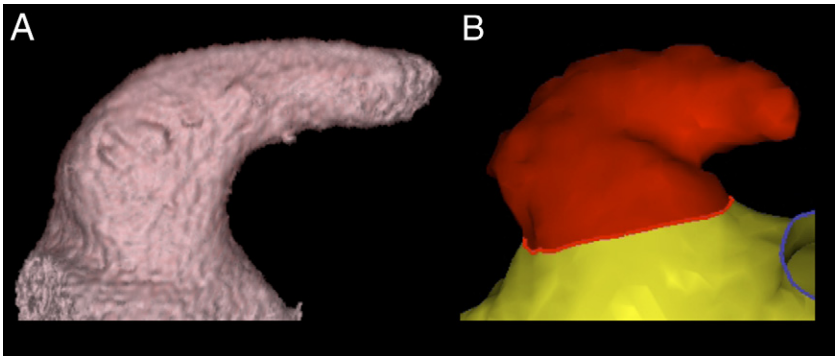

Figure 2 **CT and MRI Scans of a Chicken Wing LAA Morphology**

The Chicken Wing LAA morphology presents an obvious bend in the proximal or middle part of the dominant lobe, or folding back of the LAA anatomy on itself at some distance from the perceived LAA ostium. This type of LAA may have secondary lobes or twigs. CT **(A)** and MRI **(B)**. Abbreviations as in Figure 1.

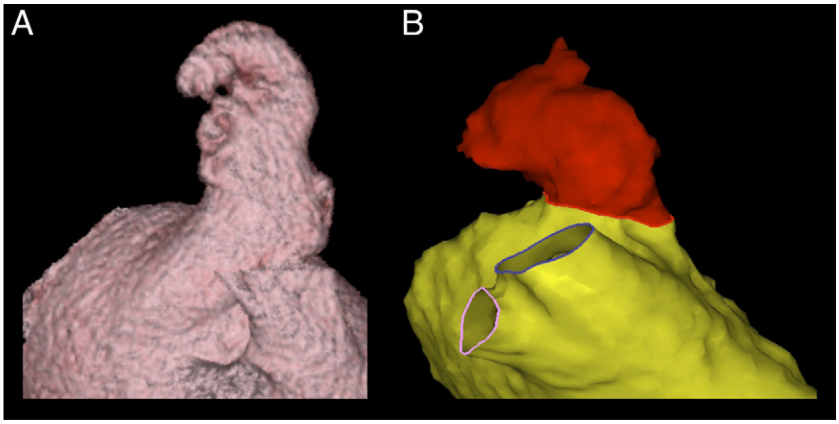

Figure 3 **CT and MRI Scans of a Windsock LAA Morphology**

The Windsock LAA morphology presents one dominant lobe of sufficient length as the primary structure. Variations of this LAA type arise with the location and number of secondary or even tertiary lobes arising from the dominant lobe. CT **(A)** and MRI **(B)**. Abbreviations as in Figure 1.

Standard measurements of LAA volume and diameters were obtained after volume rendering and integration in the Polaris image processing package of the Carto-Merge system (Biosense Webster, Diamond Bar, California). LAA morphologies were determined by 2 expert cardiac MRI radiologists who were blinded to the clinical data and history of stroke/TIA.

Classification of LAA morphology. On the basis of its morphologies, the LAA was classified as follows:

1. The Cactus LAA, with a dominant central lobe with secondary lobes extending from the central lobe in both superior and inferior directions (Fig. 1).

2. The Chicken Wing LAA, with an obvious bend in the proximal or middle part of the dominant lobe, or folding back of the LAA anatomy on itself at some distance from the perceived LAA ostium. This type of LAA may have secondary lobes or twigs (Fig. 2).

3. The Windsock LAA, with 1 dominant lobe of sufficient length as the primary structure. Variations of this LAA type arise with the location and number of secondary or even tertiary lobes arising from the dominant lobe (Fig. 3).

4. The Cauliflower LAA, with limited overall length with more complex internal characteristics. Variations of this LAA type have a more irregular shape of the LAA ostium

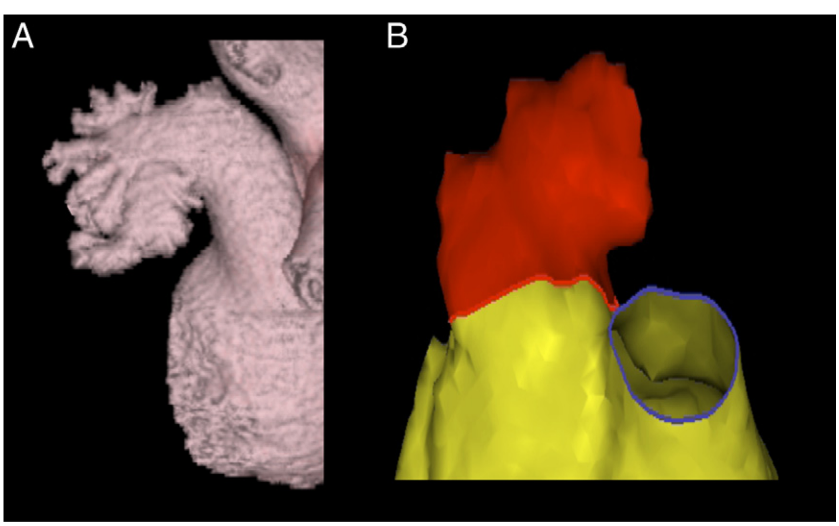

Figure 4 **CT and MRI Scans of a Cauliflower LAA Morphology**

The Cauliflower LAA morphology presents limited overall length with more complex internal characteristics. Variations of this LAA type have a more irregular shape of the LAA ostium (oval vs. round) and a variable number of lobes with lack of a dominant lobe. CT **(A)** and MRI **(B)**. Abbreviations as in Figure 1.

(oval vs. round) and a variable number of lobes with lack of a dominant lobe (Fig. 4).

Statistical analysis. All continuous data are presented as mean ± SD and were compared using analysis of variance or Kruskal–Wallis test where appropriate. Categoric variables are described as count and percent and compared by using Pearson's chi-square or Fisher exact test. Images in both modalities were independently assessed by 2 radiologists who classified those into 4 mutually exclusive LAA morphological categories. Interobserver agreement between the readers (for each modality) was evaluated using Cohen's kappa. The kappa statistic estimates the proportion of agreement among raters that exceeds the occurrence due to chance. A larger kappa value implies stronger agreement, with $\kappa = 1$ being the perfect agreement. A good level of agreement was defined as $\kappa \geq 0.61$ (14).

Multivariable logistic model was used for identifying significant predictors of stroke/TIA. All potential confounders were entered into the model on the basis of known clinical relevance or significant association observed in univariate analysis. The controlling variables used in the model were age, gender, hypertension, diabetes, AF types, LA size, and $CHADS_2$ score. On the basis of the $CHADS_2$ score before the occurrence of the thromboembolic event, the study population was stratified into 2 subgroups (i.e., $CHADS_2$ score 0 to 1 and ≥2), and a subanalysis was performed to investigate the possible association of LAA types with subsequent stroke/TIA within each group. The odds ratio (OR) and 95% confidence interval (CI) of stroke/TIA were computed. All tests were 2-sided, and a p value <0.05 was considered statistically significant. Analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

Computed tomography images of 499 patients and MRI images of 433 patients (age 59 ± 10 years, 79% were male, body mass index of 27 ± 4 kg/m^2, ejection fraction of 60 ± 7%, and 14% with a $CHADS_2$ score ≥2) presenting for catheter ablation of AF were prospectively collected. The prevalence of Cactus, Chicken Wing, Windsock, and Cauliflower types was 278 (30%), 451 (48%), 179 (19%), and 24 (3%) in the overall population; 152 (30%), 248 (50%), 89 (18%), and 10 (2%) among patients with CT; and 126 (29%), 203 (47%), 90 (21%), and 14 (3%) among those with MRI, respectively. No statistically significant bias was noted in classifying LAA morphology by operators using CT (kappa = 0.84; 95% CI: 0.61 to 0.96, $p < 0.01$) and MRI (kappa = 0.67; 95% CI: 0.48 to 0.87, $p < 0.01$). An optimal level of concordance was observed when comparing the rates of agreement for Chicken Wing and non–Chicken Wing ($\kappa = 0.91$, 0.68 to 0.96 for MRI and $\kappa = 0.96$, 0.74 to 0.98 for CT).

Table 1 presents the baseline demographic, clinical characteristics, and LAA measurements for the population sorted according to the 4 LAA types. No differences were found in the prevalence of congestive heart failure, hypertension, diabetes, dyslipidemia, or coronary artery disease. The groups were different with respect to gender, history of stroke/TIA, and $CHADS_2$ score ≥2. The Windsock type was more likely to be male. Chicken Wing was the most prevalent LAA morphology (48%). Compared with non–Chicken Wing categories, Chicken Wing had the lowest prevalence of prior stroke/TIA (4% vs. 12%, $p < 0.001$) and the least number of patients with $CHADS_2$ score ≥2 (9% vs. 18%, $p < 0.001$). No difference was noted for echocardiographic parameters (e.g., LA diameter and left ventricular ejection fraction).

Prevalence of pre-procedure stroke/TIA. In the study cohort, 78 (8%) of the 932 patients had a history of stroke/TIA before AF ablation. The distribution of the event (stroke/TIA) was significantly different across the LAA types: 35 (12%), 20 (4%), 19 (10%), and 4 (18%) for Cactus, Chicken Wing, Windsock, and Cauliflower, respectively ($p < 0.001$) (Fig. 5A). Compared with Chicken Wing, stroke/TIA events were significantly more prevalent in the non–Chicken Wing categories (4% vs. 12%, $p < 0.001$) (Fig. 5B).

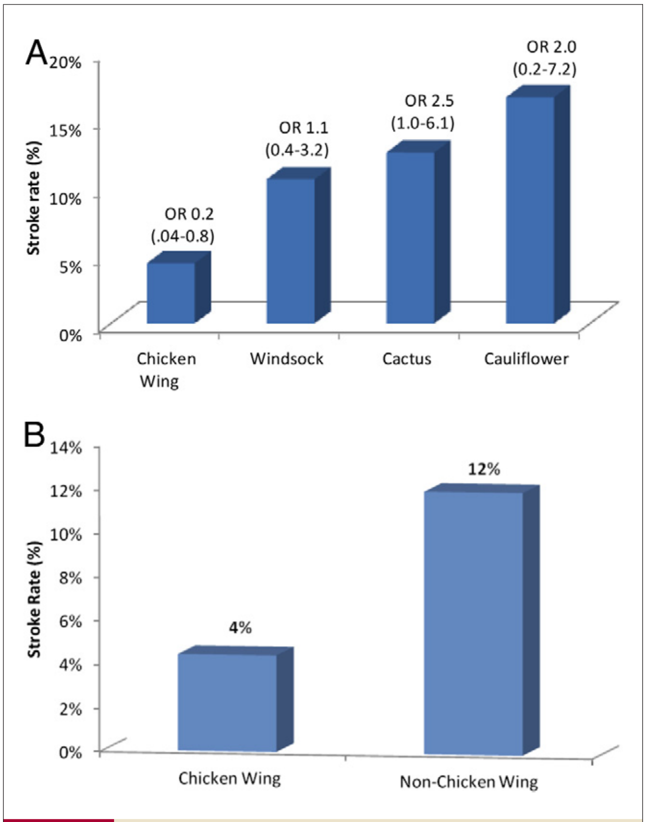

Figure 5 **Prevalence of Prior Stroke/TIA According to Different LAA Morphologies and in Chicken Wing Versus Non–Chicken Wing Morphologies**

(A) Vertical bars represent the prior stroke/TIA event rate with the univariate OR (95% CI) shown on top of the bars. **(B)** Vertical bars represent the prior stroke/TIA event rate in Chicken Wing and Non–Chicken Wing morphologies. Non–Chicken Wing was found to be an independent predictor of stroke with an OR of 2.95 (95% CI: 1.75 to 4.99, p = 0.041). OR = odds ratio.

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Table 2 Baseline Characteristics According to Event (Stroke/TIA)

	No History of Stroke/TIA	Prior Stroke/TIA	p Value
Total (N = 932)	854	78	
Age, yrs	58 ± 10	62 ± 8	0.304
Male	674 (79%)	60 (76%)	0.679
LAA type			
Cactus	243 (28%)	35 (44%)	0.002
Chicken Wing	431 (50%)	20 (26%)	<0.001
Windsock	160 (19%)	19 (24%)	0.228
Cauliflower	20 (2%)	4 (5%)	0.137
AF type			
Paroxysmal	497 (58%)	51 (66%)	0.217
Persistent	313 (37%)	23 (30%)	0.207
Long-standing persistent	44 (5%)	4 (5%)	1.00
AF duration, months	36 (12–85)	36 (24–79)	0.721
BMI	27 ± 04	27 ± 04	0.908
Dyslipidemia	193 (23%)	25 (32%)	0.059
Hypertension	409 (48%)	41 (53%)	0.429
CHF	39 (5%)	3 (4%)	0.769
Diabetes	35 (4%)	5 (6%)	0.335
CAD	43 (5%)	2 (3%)	0.330
$CHADS_2$ = 0–1*	783 (92%)	21 (27%)	<0.001
$CHADS_2$ ≥2*	71 (8%)	57 (73%)	<0.001
LVEF, %	58 ± 08	60 ± 07	0.140
LAA volume	14.13 ± 06.04	15.04 ± 07.10	0.372
LAA velocity, mm	74.77 ± 25.93	72.26 ± 20.23	0.220

Values are n, mean ± SD, n (%), or median (interquartile range). *The reported $CHADS_2$ scores have been calculated before any thromboembolic event.
Abbreviations as in Table 1.

Table 2 compares the clinical characteristics of patients with and without stroke/TIA history. The Cactus type was significantly more likely to have had a stroke (44% with stroke had Cactus type, whereas 28% of stroke-free patients had Cactus morphology, p = 0.002). Chicken Wing was strongly associated with absence of history of stroke (p < 0.001).

Univariable analysis. As revealed from univariable analysis, patients with history of stroke/TIA were more likely to have Cactus type LAA (OR 2.5, 95% CI: 1.02 to 6.08, p = 0.045) and $CHADS_2$ score ≥2 (OR 24, 95% CI: 9.93 to 60.8, p < 0.001), and those with Chicken Wing morphology were significantly less likely to have had stroke/TIA (OR 0.18, 95% CI: 0.04 to 0.77, p = 0.021). The OR and 95% CI for baseline risk factors are shown in Table 3.

Multivariable analysis. A regression model was built by adding all the covariates mentioned in the "Statistical Analysis" section. While assessing independence among the explanatory variables, a significant correlation was observed between $CHADS_2$ score and its components (i.e., age, hypertension, and diabetes). $CHADS_2$ was retained in the model, and age, hypertension, and diabetes were excluded. After controlling for $CHADS_2$ score, gender, LA size, and AF types in a multivariable logistic model, Chicken Wing was found to be 79% less likely to have a stroke/TIA history (OR 0.21, 95% CI: 0.05 to 0.91, p = 0.036). Results remained unchanged also when replacing the $CHADS_2$ score with the novel Congestive heart failure, Hypertension, Age (>75 = 2 points, 65 to 74 = 1 point, <65 = 0 point, Diabetes mellitus, prior Stroke or transient ischemic attack, female gender [CHA_2DS_2-VaSc]) score.

In a separate multivariate model, we entered Chicken Wing as the reference group and assessed the likelihood of stroke/TIA in other groups in relation to reference. Compared with Chicken Wing, Cactus was 4 times (OR 4.08, 95% CI: 1.04 to 17.27, p = 0.046), Windsock was 5 times (OR 4.8, 95% CI: 1.89 to 22.50, p = 0.038), and Cauliflower was 8 times (OR 8.02, 95% CI: 0.92 to 27.86, p = 0.056) more likely to have a stroke/TIA history. Overall, the OR for stroke/TIA in non–Chicken Wing LAA morphology was 2.95 (95% CI: 1.75 to 4.99, p = 0.041) compared with Chicken Wing.

LAA morphology and risk of prior stroke/TIA in low-risk patients. Among patients with a $CHADS_2$ score 0 to 1, Chicken Wing LAA had the lowest risk of previous stroke/TIA. Stroke was significantly more prevalent in non–Chicken Wing morphology compared with the Chicken Wing category (4.6% vs. 0.7%, p = 0.001). After adjusting for gender, AF type, and LA size, non–Chicken Wing morphology was found to be an independent predictor of stroke (OR 10.1, 95% CI: 1.25 to 79.7, p = 0.019) (Fig. 6).

LAA morphology and risk of prior stroke/TIA in patients with $CHADS_2$ score ≥2. In the cohort with a $CHADS_2$ score ≥2, although stroke was more frequently observed in the non–Chicken Wing (46% vs. 29%, p = 0.061) population, the difference did not reach statistical significance. In this regard, it is important to emphasize that patients with a $CHADS_2$ score ≥2 constituted only 14% of the entire patient cohort, and as such the study might be underpowered to disclose statistically significant differences within this subgroup.

Table 3 Univariate OR for Stroke/TIA

Variable	OR 95% CI	p Value
Age, yrs	1.04 (1.00–1.09)	0.045
Age >75 yrs	3.50 (1.69–17.54)	0.012
Male	1.17 (0.51–2.68)	0.708
LAA type		
Cactus	2.50 (1.02–6.08)	0.045
Chicken Wing	0.18 (0.04–0.77)	0.021
Windsock	1.13 (0.40–3.17)	0.821
Cauliflower	1.99 (0.23–17.23)	0.534
$CHADS_2$ ≥2	24.48 (6.93–60.84)	<0.001
BMI	1.03 (0.94–1.13)	0.562
Dyslipidemia	1.60 (0.75–3.40)	0.225
Hypertension	1.23 (0.61–2.47)	0.571
CHF	1.25 (0.28–5.61)	0.771
Diabetes	1.40 (0.31–6.35)	0.659
CAD	1.16 (0.46–3.63)	0.691
LA diameter, mm	1.06 (0.982–1.39)	0.683
LVEF, %	0.95 (0.91–1.00)	0.050
LAA volume	1.02 (0.94–1.11)	0.609
LAA velocity, mm	1.00 (0.98–1.02)	0.681

Note: The reference group for the LAA type was all the other remaining LAA morphologies.
CI = confidence interval; LA = left atrium; OR = odds ratio. Other abbreviations as in Table 1.

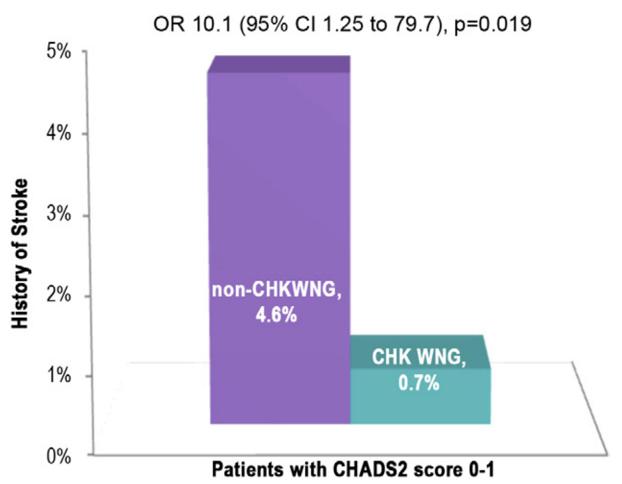

Figure 6 **Prevalence of Stroke/TIA Across Chicken Wing and Non–Chicken Wing Morphologies in $CHADS_2$ Score 0 to 1**

The columns show that Non–Chicken Wing LAA morphology increases the risk of prior stroke/TIA more than 6-fold compared with Chicken Wing (OR 10.1, 95% CI: 1.25 to 79.7, p = 0.019). $CHADS_2$ = Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack; CI = confidence interval; OR = odds ratio.

Discussion

This is the first study to correlate different LAA morphologies as obtained with CT or MRI images with the risk of prior TIA/stroke. We found that patients with the Chicken Wing LAA morphology have a statistically significant lower risk of previous stroke/TIA when compared with all the remaining LAA morphology described. The Chicken Wing LAA morphology was the most prevalent (48% of our population) and the least associated with history of stroke/TIA.

These results are novel and could be clinically relevant, especially for patients currently judged to be at low risk of thromboembolic events, such as those with $CHADS_2$ scores of 0 and 1. In these patients, the presence of a non–Chicken Wing LAA morphology strikingly increases the risk of prior thromboembolic events (up to 4.6%, corresponding to a 10-fold increased risk of prior stroke/TIA), which suggests the appropriateness of a more aggressive antithrombotic therapy. Further, this study may provide insights into why stroke/TIA has been described in patients judged to be at low risk of thromboembolism ($CHADS_2$ score of zero).

The physician and technician acquiring the CT and MRI images were blinded to the patient's history, which minimizes the risk of bias; in addition, all the statistical analyses were corrected for all possible confounders and demonstrated no interaction between the $CHADS_2$ score and the risk of prior stroke/TIA linked to different LAA morphologies.

Anatomic and mechanical concepts. The LAA is an embryological remnant that functions during conditions of fluid overload as a reservoir (6). Because of its hooked morphology, the LAA is prone to stasis and for this reason represents the prevalent site of thrombus formation in patients with AF (6). Several variables have been described to be associated with thrombus formation.

With the use of transesophageal evaluations, Leung et al. (1) and Manning et al. (7) reported that up to 98% of atrial thrombi occurring during AF derive from the LAA.

The LAA size is associated with increased thromboembolic risk (15). Autopsy studies have reported a direct association between the LAA size and the risk for stroke/TIA, especially in patients with nonvalvular AF (16,17). In our study, no significant correlation between the LAA size and the risk of prior stroke/TIA was found (Table 2). To date, there are no data correlating the various LAA morphologies with the thromboembolic risk of stroke/TIA in patients with AF.

Anticoagulation management. The $CHADS_2$ score was introduced into guidelines and implemented into clinical practice to assess individual thromboembolic risk in patients with AF. In patients with $CHADS_2$ score >1, the need for oral anticoagulation is not questionable, but in patients with low-intermediate risk for stroke ($CHADS_2$ score = 1) no consensus exists on whether patients should receive oral anticoagulation or antiplatelet therapy (18,19). With the aim to reduce the risk for stroke in patients with AF and to identify a greater number of patients at risk, a new score has been proposed by the European guidelines: the CHA_2DS_2-VaSc score (20). Although a greater number of patients are required to use oral anticoagulation with this new score, the clinical decision making is still controversial in patients with a low-risk CHA_2DS_2-VaSc score; the implementation of LAA morphology may aid the clinical decision toward oral anticoagulant or antiplatelet therapy.

It should not be forgotten that the risk for stroke should be balanced with the risk for bleeding, which is another dramatic complication in patients with AF treated with anticoagulants.

In patients with a contraindication to warfarin or because of physician and/or patient preference, it is possible to use antiplatelet therapy, although with contrasting results (18–20). In this scenario, the identification of an appendage morphology associated with a lower risk for stroke may further guide the clinicians in the decision process.

The present study suggests that the LAA morphology might be taken into account when planning the anticoagulation management of patients with AF. The LAA morphology remained the most powerful independent predictor of stroke/TIA after adjustment for the $CHADS_2$ score at multivariable regression analysis, which further strengthens the relevance of our findings. Of note, LAA morphology was confirmed to be a powerful predictor of thromboembolic events in the subgroup of patients with a low-intermediate baseline risk of stroke/TIA, such as those with $CHADS_2$ scores of 0 to 1. Moreover, from a practical perspective, our data suggest that it is important to correctly recognize only patients with Chicken Wing LAA morphology, which is the most prevalent and easiest to detect. Indeed, the risk of prior stroke/TIA was similar across all other LAA morphologies. This information facilitates the clinical decision making with regard to the antithrombotic therapy.

The advent of the new oral anticoagulants with improved thromboembolic protection, lower risk of bleeding, and better patient compliance may justify the appropriateness of early antithrombotic therapy in patients at lower risk of thromboembolic events and non–Chicken Wing LAA morphology (21–23). The cost-effectiveness of such anticoagulation management when compared with warfarin requires further investigation.

Study limitations. Although the study was retrospective, it included a large sample size. Furthermore, our data derive from a selected population of patients undergoing AF ablation, and further studies are necessary to establish whether our results might be extended to the general population with AF.

We were unable to retrieve the anticoagulation status at the time of the event, which represents a significant limitation especially in the subgroup of patients at high risk of stroke (i.e., $CHADS_2$ scores ≥2). Although this might be considered a major limitation, the strong independent statistical association between LAA morphology and risk of prior stroke is of utmost clinical relevance.

Conclusions

This study suggests that patients with non–Chicken Wing LAA morphology are significantly more likely to have an embolic event, even after controlling for comorbidities and $CHADS_2$ score. If confirmed, these results could have a relevant impact on the anticoagulation management of patients with AF, especially of those with an intermediate-low risk for stroke (i.e., $CHADS_2$ score 0 to 1) in whom oral anticoagulant therapy is currently not recommended.

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