Anatomical characteristics of the left atrium and left atrial appendage in relation to the risk of stroke in patients with versus without atrial fibrillation

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ORIGINAL ARTICLE

Anatomical Characteristics of the Left Atrium and Left Atrial Appendage in Relation to the Risk of Stroke in Patients With Versus Without Atrial Fibrillation

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BACKGROUND: The left atrial appendage (LAA) has been regarded as an important source of cardiac thrombus formation and appears important in the contribution to thromboembolism in patients with atrial fibrillation (AF). Our aim was to evaluate the relationship between LAA morphology and previous stroke or transient ischemic attack in 2 large and distinct patient cohorts with and without known AF.

METHODS: The study population consisted of patients with and without drug-refractory AF who underwent computed tomography before transcatheter AF ablation or clinically indicated for suspected coronary artery disease. The computed tomography data were used for volumetric assessment of the left atrium and LAA and to determine LAA morphology. The LAA was classified by 3 readers in consensus as chicken wing, swan, cauliflower, or windsock, based on predefined morphology classification criteria.

RESULTS: In total, 1813 patients (mean age 59±11 years, 42% female) who underwent computed tomography were included in this analysis (908 patients with AF and 905 patients without known AF). Swan LAA morphology was independently associated with prior stroke/transient ischemic attack in the overall study population (odds ratio, 3.40, $P<0.001$), and in patients with (odds ratio, 2.88, $P=0.012$) and without known AF (odds ratio, 3.96, $P=0.011$).

CONCLUSIONS: Swan morphology of the LAA is independently associated with prior stroke or transient ischemic attack in patients with known AF, as well as in patients not previously diagnosed with AF.

GRAPHIC ABSTRACT: An online graphic abstract is available for this article.

Key Words: atrial appendage ■ atrial fibrillation ■ computed tomography ■ stroke ■ thromboembolism

Atrial fibrillation (AF) is the most common sustained rhythm disorder worldwide.[1] AF is known to be associated with a 5-fold increased risk of stroke or transient ischemic attack (TIA) as compared to patients without known AF.[2] The left atrial appendage (LAA) has been regarded as an important source of cardiac thrombus formation and appears important in the contribution to thromboembolism in patients with AF. The structure of the LAA is known to be diverse and different morphologies have been proposed in an attempt to classify this highly unique structure.[3,4] Over the recent years, computed tomography (CT) has been shown to be an accurate imaging technique to assess LAA morphology. Prior CT studies have shown a clear

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WHAT IS KNOWN?

- The left atrial appendage has been regarded as an important source of cardiac thrombus formation and appears important in the contribution to thromboembolism in patients with atrial fibrillation.
- Prior computed tomography studies have shown a clear correlation between left atrial appendage morphology and the occurrence of previous stroke or transient ischemic attack in patients with atrial fibrillation.

WHAT THE STUDY ADDS

- Our study is the first to investigate the relationship between the swan left atrial appendage morphology and prior stroke and/or transient ischemic attack.
- Swan morphology of the left atrial appendage is associated with prior stroke or transient ischemic attack in patients with atrial fibrillation, as well as in patients with known or suspected coronary artery disease who were not previously diagnosed with atrial fibrillation.

Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
CAD	coronary artery disease
LA	left atrium
LAA	left atrial appendage
OR	odds ratio
TIA	transient ischemic attack

correlation between LAA morphology and the occurrence of previous stroke or TIA in patients with AF.[4–7] However, the relation between LAA morphology and the risk of stroke or TIA has not been assessed in large, distinct patient cohorts or in patients without known AF. In the current study, we have evaluated the relationship between LAA morphology (assessed by CT) and previous stroke or TIA in 2 large and distinct patient cohorts from Leiden University Medical Center (Leiden, the Netherlands) and Semmelweis University (Budapest, Hungary). Each patient cohort consisted of 2 groups: Group (1) Patients with a history of AF and Group (2) Patients with known or suspected coronary artery disease (CAD) who were not previously diagnosed with AF.

METHODS

Patients

The data that support the findings of this study are available from the corresponding author upon reasonable request. The study population consisted of 2 groups: Group (1) Patients with drug-refractory AF who underwent CT before transcatheter AF ablation (in these patients, CT was clinically indicated for evaluation of the size, and anatomy of the left atrium [LA], pulmonary veins, and the LAA) and group (2) patients without documented AF who underwent clinically indicated coronary CT angiography for suspected CAD.

The presence and pattern of AF were defined according to the European Society of Cardiology Guidelines for the management of AF.[8] The primary outcome parameter of the current study was prior stroke or TIA, which was defined as the presence of ischemic stroke or TIA (ie, hemorrhagic strokes were excluded). Patient data were collected from 2 sites: Leiden University Medical Center (Leiden, The Netherlands) and Heart and Vascular Center, Semmelweis University (Budapest, Hungary).

The CT data were used for volumetric assessment of the LA and LAA and to determine LAA morphology. Only patients with complete visualization of the LAA on CT without filling defects or severe motion artifacts were included. Clinical data, including the history of stroke or TIA, were prospectively entered in the electronic patient file and retrospectively analyzed. For retrospective analysis of clinically acquired data, the institutional review boards of both sites waived the need of written patient informed consent. All data used for this study were acquired for clinical purposes and were handled in a coded fashion.

Coronary CT Angiography Data Acquisition

CT data acquisition was performed with a 320-slice CT scanner in Leiden, the Netherlands (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan) with a collimation of 320×0.5 mm, a temporal resolution of 175 ms, and a gantry rotation time of 350 ms. Peak tube voltage and current ranged from 100 to 135 kV and 140 to 580 mA, respectively, depending on the body mass index of the patient. To achieve an optimal heart rate (≤65 beats per minute) 25 to 150 mg metoprolol was administered orally 1 hour before the examination unless contraindicated. If the heart remained >65 beats per minute, an additional dose of metoprolol was administered intravenously (up to 15 mg). In addition, sublingual nitrates (0.8 mg) were administered before the scan to achieve vasodilation of the coronary arteries, provided that there were no contraindications. CT was performed with prospective electrocardiographic gating covering 70-80% of the RR interval. For patients with a heart rate >65 beats per minute, 30% to 80% of the RR interval was scanned to allow image reconstructions of the systolic and diastolic phases. A triphasic injection protocol was used to administer 60 to 90 mL of contrast agent (Iomeron 400, Bracco, Milan, Italy). CT data were acquired the following heartbeat after reaching the threshold of 300 HU in the descending aorta.

CT data acquisition was performed with a 256-slice CT scanner in Budapest, Hungary (Brilliance iCT 256, Phillips Healthcare, Best, the Netherlands) with 270 ms rotation time, 128×0.625 mm collimation, and tube voltage of 100 to 120 kV. Four-phasic injection protocol with 85-95 mL of iodinated contrast agent was used (Iomeron 400, Bracco Ltd; Milan, Italy) at a rate of 4.5 to 5.5 mL/s.[9] CT was acquired using prospective ECG-gating covering 75% to 81% of the RR interval. The CT data sets were reconstructed with 0.8 mm slice thickness and 0.4 mm increment with hybrid iterative reconstruction technique (iDose5, Philips Healthcare, Best, the Netherlands).

CT Data Analysis

Volumetric assessment of the LA and LAA was performed on CT data using a dedicated software package (IntelliSpace Portal, Philips Healthcare, Eindhoven, the Netherlands, version 10.1). Image reconstructions of the diastolic phase (ie, 70%–80% of the cardiac cycle) were used for the analysis. The LA and LAA borders were semiautomatically traced to obtain a 3-dimensional volume rendered image of the LA and LAA (Figure 1). These images were manually corrected taking into consideration the following prespecified anatomic landmarks: the orifices of the pulmonary veins, the mitral annulus (differentiating the LA from the left ventricle) and the ostium of the LAA. Subsequently, the LAA was classified into the 4 different types according to its morphology, as described previously.[3] The LAA morphology was determined by 3 readers in consensus, who were all blinded to the clinical data and the history of stroke or TIA. The LAA was classified as follows:

1. Chicken wing, if the LAA presented an obvious bend in the proximal or middle part of the dominant lobe with the distal part completely overriding the perceived ostium of the LAA (Figure 2A).
2. Swan, if the LAA presented a second sharp curve folding the structure back (Figure 2B).
3. Cauliflower, if the LAA presented a limited overall length and a distal width exceeding the proximal width (Figure 2C).
4. Windsock, if the LAA presented one dominant lobe of sufficient overall length (Figure 2D).

Statistical Analysis

Distribution of continuous variables was determined using histograms and normal Q-Q plots. Continuous variables are presented as mean±SD and were compared with the independent sample Student *t* test. Categorical variables are presented as number and percentages and were compared with the χ^2 test or Fisher exact test if 5 or less observations were included in a subclass. Univariable logistic regression analysis was performed to assess the association between anatomic characteristics of the LA and LAA and prior stroke/TIA. In addition, multivariable analysis was performed to adjust for variables from the CHA2DS2-VASc score (ie, heart failure, hypertension, age, diabetes, vascular disease, and sex).[8] All variables with a $P<0.10$, and the LAA morphology most strongly associated with prior stroke/TIA in the univariable analysis, were included in the multivariable analysis. Statistical analysis was performed with the SPSS software package (IBM Corp Released 2015; IBM SPSS Statistics for Windows, Version 25.0; Armonk, New

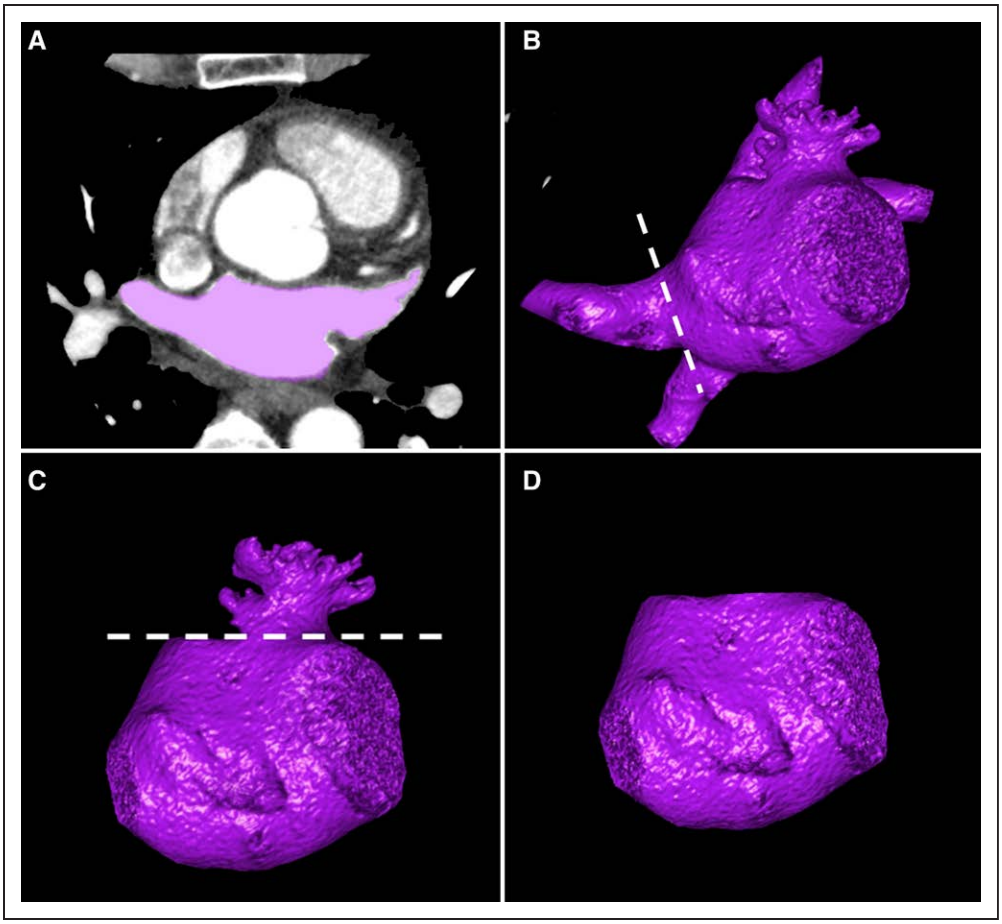

Figure 1. Semiautomated volumetric assessment of the left atrial (LA) and left atrial appendage (LAA).
A, The LA and LAA borders were semiautomatically traced to obtain a 3-dimensional (3D) volume rendered image of the LA and LAA. **B**, The pulmonary veins were manually excluded at their orifices from the LA on the 3-dimensional (3D) image. The mitral annulus was used as an anatomic landmark to differentiate the LA from the left ventricle. **C**, The combined volume of the LA and LAA was calculated and LAA morphology was assessed. Subsequently, the LAA was excluded at its ostium from the LA on the 3D image. **D**, The volume of the LA (excluding the pulmonary veins and LAA) was calculated. To obtain the LAA volume, the LA volume was subtracted from the combined volume of the LA and LAA.

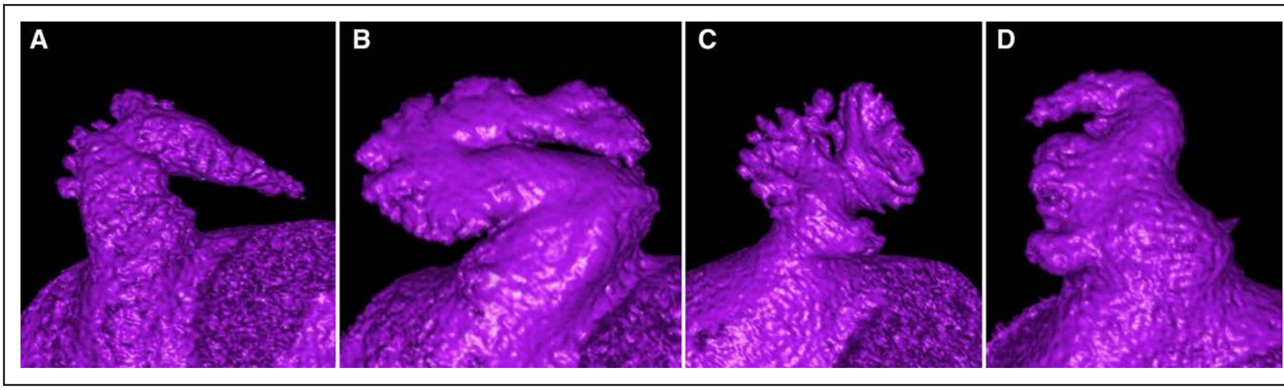

Figure 2. Examples of the 4 different types of left atrial appendage (LAA) morphology classified on computed tomography (CT). **A**, Chicken wing LAA morphology, presenting an obvious bend in the proximal or middle part of the dominant lobe with the distal part completely overriding the perceived ostium of the LAA. **B**, Swan LAA morphology, presenting a second sharp curve folding the structure back. **C**, Cauliflower LAA morphology, presenting a limited overall length and a distal width exceeding the proximal width. **D**, Windsock LAA morphology, presenting one dominant lobe of sufficient overall length.

York: IBM Corp). Statistical tests were considered significant if the 2-sided *P* value was <0.05.

RESULTS

Patients

In total, 1813 patients who underwent CT were included in this analysis (908 patients with AF and 905 patients without known AF). Mean age of the population was 59±11 years and 42% of the patients were female (Table 1). Patients with AF were significantly older ($P<0.001$), predominantly male ($P<0.001$) and had a higher prevalence of hypertension ($P<0.001$), obesity ($P=0.018$), and vascular disease ($P=0.011$) compared with patients without known AF. A complete overview of the baseline characteristics is shown in Table 1.

Anatomic Characteristics of the LA and LAA According to AF Status

Mean LA and LAA volume were 94±31 and 7.7±4.3 mL, respectively, in the overall population (Table 1). In patients

Table 1. Baseline Characteristics According to AF Status

	Overall population (n=1813)	Patients with AF (n=908)	Patients without known AF (n=905)	*P* value
Age, y	59±11	61±10	56±12	<0.001*
Female	758 (42%)	300 (33%)	458 (51%)	<0.001*
Hypercholesterolemia	499 (28%)	202 (22%)	297 (33%)	<0.001*
Hypertension	952 (53%)	513 (57%)	439 (49%)	<0.001*
Diabetes	180 (10%)	99 (11%)	81 (9%)	0.14
Obesity (BMI≥30)	347 (20%)	190 (22%)	157 (18%)	0.018*
Current smoker	442 (25%)	219 (26%)	223 (25%)	0.68
Family history of CAD	473 (27%)	116 (14%)	357 (40%)	<0.001*
Obstructive CAD (≥50%)	174 (10%)	75 (8%)	99 (11%)	0.053
Congestive heart failure	15 (1%)	8 (1%)	7 (1%)	0.80
Vascular disease	148 (8%)	89 (10%)	59 (7%)	0.011*
Persistent AF	NA	171 (19%)	NA	
LA volume, mL	94±31	109±32	78±20	<0.001*
LAA volume, mL	7.7±4.3	8.8±5.3	6.6±2.5	<0.001*
LAA morphology				
Chicken wing	206 (11%)	110 (12%)	96 (11%)	0.31
Cauliflower	953 (53%)	469 (52%)	484 (54%)	0.44
Windsock	582 (32%)	286 (32%)	296 (33%)	0.58
Swan	72 (4%)	43 (5%)	29 (3%)	0.095

AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; LA, left atrial; LAA, left atrial appendage; and NA, not available.

*Values indicate statistically significant results.

Table 2. Distribution of LAA Morphology Across 10-Year Age Groups

Age groups	Chicken wing	Cauliflower	Windsock	Swan	Total
<50	38 (18.4%)	191 (20.0%)	135 (23.2%)	18 (25.0%)	382 (21.1%)
50–59	48 (23.3%)	266 (27.9%)	183 (31.4%)	15 (20.8%)	512 (28.2%)
60–69	72 (35.0%)	327 (34.3%)	180 (30.9%)	27 (37.5%)	606 (33.4%)
≥70	48 (23.3%)	169 (17.7%)	84 (14.4%)	12 (16.7%)	313 (17.3%)
Total	206 (100%)	953 (100%)	582 (100%)	72 (100%)	1813 (100%)

Pearson χ^2 P=0.045. LAA indicates left atrial appendage.

with AF, LA and LAA volume were significantly larger compared with patients without known AF (LA volume: 109±32 versus 78±20 mL, P<0.001 and LAA volume: 8.8±5.3 versus 6.6±2.5 mL, P<0.001). Cauliflower was the most prevalent LAA morphology (53%) in the overall study population, followed by windsock (32%), chicken wing (11%), and swan LAA morphology (4%). Chicken wing morphology was more prevalent at higher age groups (18.4% in age group <50 versus 23.3% in age group ≥70 years), while windsock morphology showed to be more prevalent at lower age groups (23.2% in age group <50 versus 14.4% in age group ≥70 years; Table 2). CHA2DS2-VASc score (Table 3) and anticoagulant status (Table 4) were not significantly different between patients with the 4 types of LAA morphology. No significant difference was found in LAA morphology between patients with versus without known AF (chicken wing: 12% versus 11%, P=0.31; cauliflower: 52% versus 54%, P=0.44; windsock: 32% versus 33%, P=0.58; and swan: 5% versus 3%, P=0.095; Figure 3).

Anatomic Characteristics of the LA and LAA According to Prior Stroke/TIA

In total, 120 (7%) patients had a history of stroke or TIA (73 patients with AF and 47 patients without known AF). In patients with AF, LA and LAA volume were not significantly different between patients with and without prior stroke/TIA (LA volume: 114±32 versus 108±31 mL, P=0.16 and LAA volume: 9.2±5.3 versus 8.7±5.3 mL, P=0.47; Table 5). In patients without known AF, LA volume was significantly higher in patients with prior stroke/TIA (86±23 versus 78±20 mL, P=0.011), while no significant difference was found for LAA volume (6.9±2.5 versus 6.6±2.5 mL, P=0.39). Both in patients with and without known AF, the prevalence of chicken wing, cauliflower, and windsock LAA morphology was not significantly different between patients with and without prior stroke/TIA. In contrast, swan LAA morphology was significantly more prevalent in patients with prior stroke/TIA, both in patients with (11% versus 4%, P=0.009) and without known AF (11% versus 3%, P=0.003).

LAA Morphology in Relation to Prior Stroke/TIA

The stroke/TIA rate was the highest in patients with a swan LAA morphology in the overall study population (swan 18% versus chicken wing 4% versus cauliflower 7% versus windsock 6%), as well as in patients with AF (swan 19% versus chicken wing 6% versus cauliflower 8% versus windsock 7%) and without known AF (swan 17% versus chicken wing 1% versus cauliflower 6% versus windsock 4%; Figure 4). Multivariable analysis showed an independent association between swan LAA morphology and prior stroke/TIA in the overall study population (odds ratio [OR], 3.40, P<0.001), and in patients with (OR, 2.88, P=0.012) and without known AF (OR, 3.96, P=0.011; Table 6). Also, swan morphology remained significantly associated with prior stroke/TIA corrected for the CHA2DS2-VASc score (excluding prior stroke or TIA) in the overall study population (OR,

Table 3. Distribution of CHA_2DS_2-VASc Score* Across 4 Types of LAA Morphology

CHA_2DS_2-VASc score	Chicken wing	Cauliflower	Windsock	Swan	Total
0	45 (22.0%)	183 (19.4%)	115 (20.0%)	20 (28.2%)	363 (20.2%)
1	65 (31.7%)	322 (34.1%)	204 (35.5%)	21 (29.6%)	612 (34.1%)
2	48 (23.4%)	243 (25.7%)	156 (27.1%)	14 (19.7%)	461 (25.7%)
3	34 (16.6%)	138 (14.6%)	76 (13.2%)	11 (15.5%)	259 (14.4%)
4	11 (5.4%)	49 (5.2%)	22 (3.8%)	5 (7.0%)	87 (4.8%)
5	2 (1.0%)	9 (1.0%)	2 (0.3%)	0 (0%)	13 (0.7%)
6	0 (0%)	1 (0.1%)	0 (0%)	0 (0%)	1 (0.1%)
7	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	205 (100%)	495 (100%)	575 (100%)	71 (100%)	1796 (100%)

Pearson χ^2 P=0.80. LAA indicates left atrial appendage.
*CHA_2DS_2-VASc score excluding prior stroke or TIA, since this is the study's outcome parameter.

Table 4. Distribution of Anticoagulant Status* Across 4 Types of LAA Morphology

OAC	Chicken wing	Cauliflower	Windsock	Swan	Total
Yes	86 (79.6%)	366 (78.5%)	222 (78.4%)	32 (76.2%)	706 (78.5%)
No	22 (20.4%)	100 (21.5%)	61 (21.6%)	10 (23.8%)	193 (21.5%)
Total	106 (100%)	466 (100%)	283 (100%)	42 (100%)	899 (100%)

Pearson χ^2 *P*=0.98. LAA indicates left atrial appendage; and OAC, oral anticoagulation.
*Anticoagulant status was defined by the use of either a direct oral anticoagulant or vitamin K antagonist.

3.50, *P*<0.001), as well as for patients with (OR, 2.92, *P*=0.010) and without known AF (OR, 4.29, *P*=0.006). Although LA volume was independently associated with prior stroke/TIA in the overall study population (OR per 1 mL increase 1.007, *P*=0.029), no independent association was found for LA and LAA volume when subdivided to AF status.

DISCUSSION

In the current study, we showed in 2 large and distinct patient cohorts that LAA morphology is associated with prior stroke or TIA, independent of clinical risk factors. Swan morphology of the LAA was associated with prior stroke or TIA in patients with AF with a 3- to 4-fold OR, as well as in patients with known or suspected CAD who were not previously diagnosed with AF. In addition, LAA morphology was not significantly different between patients with and without known AF.

Structure and Function of the LAA

The LAA is a finger- or stump-like structure extending from the main body of the LA.[10–14] It represents a unique structure with ample variations in size, morphology, and number of lobes. Moreover, the LAA has a close anatomic localization to the left circumflex coronary artery, left superior pulmonary vein, and mitral valve, and its relationship to these structures is known to be highly variable. Additionally, the LAA has important contractile properties which typically lead to a quadriphasic flow pattern in patients with sinus rhythm: (1) LAA contraction during late diastole, (2) LAA filling in early systole, (3) passive LAA flow during the remainder of the systole, and (4) LAA outflow during early diastole.[15] As a consequence, adequate blood flow is present within the LAA during the entire cardiac cycle, which markedly reduces the risk of blood stasis and thrombosis. However, in patients with AF, blood flow in the LAA is thought to be impaired and flow velocity (ie, the combination of LAA contraction and filling) is significantly lower compared with patients with sinus rhythm.[16] This could potentially result in stagnation of blood, thrombus formation, and eventually the occurrence of thromboembolic events.

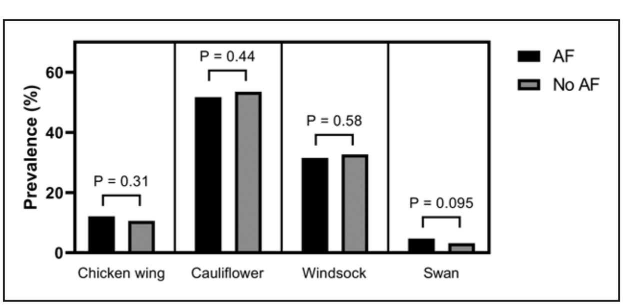

Figure 3. Distribution of the 4 different types of left atrial appendage (LAA) morphology in patients with and without known atrial fibrillation (AF).
No significant difference was found for each of the 4 different types of LAA morphology between patients with and without known AF.

LAA Morphology in Relation to Prior Stroke/TIA

Several studies have investigated the association between LAA morphology and prior stroke or TIA. Di Biase et al[4] analyzed 932 patients with drug-refractory AF who underwent cardiac CT or magnetic resonance imaging before transcatheter ablation and were screened for prior stroke or TIA. The authors showed that chicken wing LAA morphology was independently associated with a reduced risk of thromboembolic events, even after controlling for comorbidities and the $CHADS_2$ score. Moreover, multiple studies have demonstrated a relationship between any or all types of the nonchicken wing LAA morphologies (ie, cauliflower, windsock, and cactus LAA morphology) and prior stroke/TIA.[5–7] In contrast to most study results, Wu et al[17] recently found no significant relationship between LAA morphology and history of prior stroke or TIA in 2264 patients who underwent CT for assessment of LAA anatomy.[17]

Interestingly, several studies have suggested a specific LAA echocardiographic flow pattern (ie, a low flow velocity) as the underlying mechanism associating LAA morphology and stroke or TIA. Fukushima et al[18] studied 96 patients with paroxysmal AF who were referred for transcatheter ablation and underwent CT, transthoracic and transesophageal echocardiography. The authors reported that LAA flow velocity, measured by transesophageal echocardiography during sinus rhythm, was significantly higher in patients with chicken wing LAA morphology compared with the other LAA morphologies. Even after adjusting for clinical and LAA anatomic parameters, LAA morphology was shown to be an independent determinant of LAA flow velocity. The association between chicken wing LAA morphology and a higher LAA flow velocity was also confirmed by multiple other studies.[19–22]

Table 5. Baseline Characteristics According to Prior Stroke/TIA

	Overall population (n=1813)			Patients with AF (n=908)			Patients without known AF (n=905)		
	Prior stroke/TIA (n=120)	No prior stroke/TIA (n=1693)	*P* value	Prior stroke/TIA (n=73)	No prior stroke/TIA (n=835)	*P* value	Prior stroke/TIA (n=47)	No prior stroke/TIA (n=858)	*P* value
Age, y	62±10	58±11	<0.001*	64±9	61±10	0.004*	60±11	56±12	0.033*
Female	52 (43%)	706 (42%)	0.73	25 (34%)	275 (33%)	0.82	27 (57%)	431 (50%)	0.34
Hypercholesterolemia	47 (39%)	452 (27%)	0.004*	28 (38%)	174 (21%)	0.001*	19 (40%)	278 (33%)	0.26
Hypertension	75 (63%)	877 (52%)	0.030*	46 (63%)	467 (57%)	0.29	29 (62%)	410 (48%)	0.066
Diabetes	18 (15%)	162 (10%)	0.059	8 (11%)	91 (11%)	0.98	10 (21%)	71 (8%)	0.002*
Obesity (BMI≥30)	26 (22%)	321 (20%)	0.51	11 (16%)	179 (23%)	0.18	15 (32%)	142 (17%)	0.008*
Current smoker	38 (33%)	404 (25%)	0.058	23 (33%)	196 (25%)	0.15	15 (32%)	208 (24%)	0.24
Family history of CAD	27 (23%)	446 (28%)	0.32	5 (7%)	111 (14%)	0.098	22 (47%)	335 (39%)	0.30
Obstructive CAD (≥50%)	22 (18%)	152 (9%)	0.001*	11 (15%)	64 (8%)	0.028*	11 (23%)	88 (10%)	0.005*
Congestive heart failure	2 (2%)	13 (1%)	0.29	1 (1%)	7 (1%)	0.64	1 (2%)	6 (1%)	0.28
Vascular disease	18 (15%)	130 (8%)	0.005*	12 (16%)	77 (9%)	0.047*	6 (13%)	53 (6%)	0.075
Persistent AF	14 (12%)	157 (9%)	NA	14 (19%)	157 (19%)	0.95	NA	NA	NA
LA volume, mL	103±32	93±30	0.001*	114±32	108±31	0.16	86±23	78±20	0.011*
LAA volume, mL	8.3±4.5	7.6±4.3	0.11	9.2±5.3	8.7±5.3	0.47	6.9±2.5	6.6±2.5	0.39
LAA morphology									
Chicken wing	8 (7%)	198 (12%)	0.093	7 (10%)	103 (12%)	0.49	1 (2%)	95 (11%)	0.053
Cauliflower	67 (56%)	886 (52%)	0.46	38 (52%)	431 (52%)	0.94	29 (62%)	455 (53%)	0.25
Windsock	32 (27%)	550 (33%)	0.19	20 (27%)	266 (32%)	0.43	12 (26%)	284 (33%)	0.28
Swan	13 (11%)	59 (4%)	<0.001*	8 (11%)	35 (4%)	0.009*	5 (11%)	24 (3%)	0.003*

AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; LA, left atrial; LAA, left atrial appendage; NA, not available; and TIA, transient ischemic attack.

*

In our study, we found swan morphology of the LAA to be independently associated with prior stroke or TIA, both in patients with and without known AF. It could be hypothesized that swan LAA morphology, due to its curved structure, is associated with a lower flow velocity compared with other morphologies. As a consequence, swan LAA morphology may be prone to stasis of blood, leading to thrombus formation, and the occurrence of

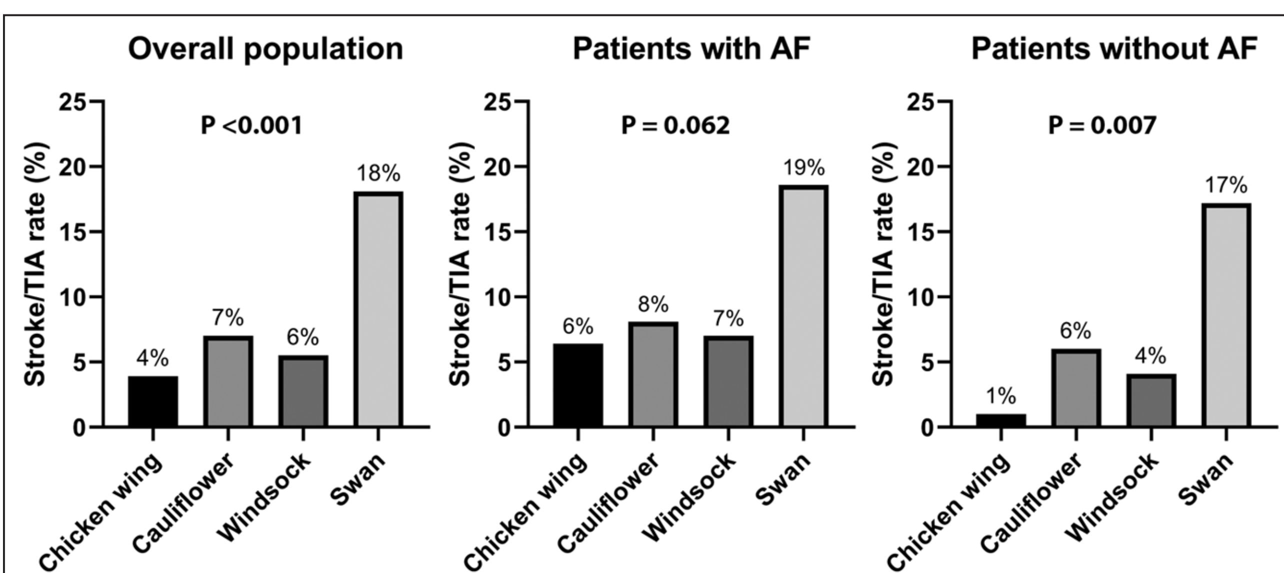

Figure 4. The stroke/transient ischemic attack (TIA) rate in the overall patient population and in patients with and without known atrial fibrillation (AF).

The stroke/TIA rate was the highest in patients with a swan left atrial appendage (LAA) morphology (18% in the overall population, 19% in patients with AF, and 17% in patients without known AF).

Table 6. Logistic Regression Analysis for Prior Stroke/TIA

	Overall population (n=1813)				Patients with AF (n=908)				Patients without known AF (n=905)			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
LA volume (per 1 mL increase)	1.009 (1.004–1.015)	0.001*	1.007 (1.001–1.013)	0.029*	1.005 (0.998–1.012)	0.16			1.017 (1.004–1.030)	0.012*	1.012 (0.998–1.027)	0.088
LAA volume (per 1 mL increase)	1.024 (0.993–1.055)	0.13			1.013 (0.978–1.049)	0.48			1.047 (0.944–1.160)	0.39		
LAA morphology†												
Chicken wing	0.54 (0.26–1.12)	0.098			0.75 (0.34–1.69)	0.49			0.18 (0.02–1.28)	0.086		
Cauliflower	1.15 (0.79–1.67)	0.46			1.02 (0.63–1.64)	0.94			1.43 (0.78–2.61)	0.25		
Windsock	0.76 (0.50–1.15)	0.19			0.81 (0.47–1.38)	0.43			0.69 (0.35–1.36)	0.28		
Swan	3.37 (1.79–6.33)	<0.001*	3.40 (1.78–6.50)	<0.001*	2.81 (1.25–6.32)	0.012*	2.88 (1.26–6.58)	0.012*	4.14 (1.50–11.38)	0.006*	3.96 (1.36–11.48)	0.011*
Congestive heart failure	2.19 (0.49–9.82)	0.31			1.64 (0.20–13.54)	0.65			3.09 (0.36–26.18)	0.30		
Hypertension	1.52 (1.04–2.23)	0.031*	1.23 (0.82–1.85)	0.31	1.30 (0.79–2.14)	0.30			1.75 (0.96–3.20)	0.069	1.37 (0.71–2.64)	0.34
Age (per 1 y increase)	1.04 (1.02–1.06)	<0.001*	1.03 (1.01–1.05)	0.009*	1.04 (1.01–1.07)	0.004*	1.04 (1.01–1.07)	0.007*	1.03 (1.00–1.06)	0.034*	1.02 (0.99–1.05)	0.32
Diabetes	1.65 (0.98–2.80)	0.062	1.46 (0.84–2.52)	0.18	0.99 (0.46–2.13)	0.98			2.98 (1.42–6.25)	0.004*	2.57 (1.18–5.62)	0.018*
Vascular disease	2.12 (1.25–3.61)	0.006*	1.73 (1.00–3.00)	0.049*	1.94 (1.00–3.75)	0.050	1.59 (0.81–3.15)	0.18	2.22 (0.90–5.47)	0.082	2.05 (0.81–5.19)	0.13
Female sex	1.07 (0.74–1.55)	0.73			1.06 (0.64–1.76)	0.82			1.34 (0.74–2.42)	0.34		

AF indicates atrial fibrillation; LA, left atrial; LAA, left atrial appendage; OR, odds ratio; and TIA, transient ischemic attack.

*

†Reference group: all other types of LAA morphology.

stroke or TIA. Although conceptually attractive, further studies are needed to investigate the echocardiographic flow pattern in swan LAA morphology and its relationship to thrombus formation and subsequent thromboembolism. As a second hypothesis, the swan LAA morphology visually resembles a dilated chicken wing morphology with an S shape. Due to its large structure's space, thrombi will not be obstructed, and the risk of migration and transit of thrombi could be higher compared with the chicken wing morphology.

The current study has several unique features compared with previous studies that determined the relationship between LAA morphology and stroke or TIA. It is the first study to investigate the relationship between the swan LAA morphology and prior stroke or TIA. The swan morphology was used instead of the cactus morphology, which visually resembles an extended cauliflower morphology. As opposed to prior studies that focused on LAA morphology and stroke/TIA, the current study included patients with suspected CAD who were not previously diagnosed with AF. Moreover, the prevalence of the chicken wing morphology was lower in the current study as compared to most studies on LAA morphology.

Study Limitations

The present study has several limitations. This is a retrospective study with all its inherent limitations. Moreover, classification of LAA morphology was based on visual assessment, which could result in a significant interobserver and intraobserver variability. In addition, patients with known or suspected CAD who were not previously diagnosed with AF, could have occult (ie, undetected) paroxysmal AF. Continuous rhythm or ambulatory ECG monitoring was not routinely performed to exclude the presence of AF in this patient group. Cultural and genetic factors of our sampled study population were not available, and therefore, its effect on the relationship between LAA morphology and prior stroke or TIA could not be assessed. Also, LAA morphology could not be accurately assessed on CT scans with filling defects or severe motion artifacts. Furthermore, thromboembolism from the LAA is only one of the suggested pathophysiologic processes causing stroke or TIA, and data on cerebrovascular diseases and carotid artery stenosis were not available. Finally, the relationship between LAA morphology and silent cerebral events could not be studied since brain imaging data were not available.

Conclusions

The current study showed that swan morphology of the LAA is independently associated with prior stroke or TIA in patients with known AF, as well as in patients not previously diagnosed with AF. Further studies are needed to investigate the pathophysiological mechanism underlying the link between swan LAA morphology and the occurrence of stroke or TIA, including the effect of LAA blood flow velocity. Moreover, future studies should incorporate a computer-based, automated assessment of LAA morphology to improve reproducibility.

ARTICLE INFORMATION

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