Malignant left atrial appendage morphology and embolization risk in atrial fibrillation

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Introduction

The risk of stroke is increased 4- to 5-fold in patients with atrial fibrillation (AF).[1] Predicting this risk is a significant clinical challenge. Despite the knowledge that most thrombi leading to cerebral embolization arise in the left atrial appendage (LAA),[2–4] physicians today rely heavily on clinical predictors (CHADS$_2$ [congestive heart failure, hypertension, age $\geq$75 y, diabetes mellitus, and prior stroke/transient ischemic attack/thromboembolism] and CHA$_2$DS$_2$-VASc [congestive heart failure, hypertension, age $\geq$75 y, diabetes mellitus, and prior stroke/transient ischemic attack/thromboembolism, vascular disease, age 65–74 y, sex category] algorithms) to stratify patients and anticoagulate accordingly.[5,6] None of these clinical predictors include factors related to the LAA or its anatomic or hemodynamic characteristics.

Recent studies have attempted to identify specific features in LAA morphology that may predispose to thromboembolism.[7–10] Here we present 2 extreme cases of recurrent thromboembolism in AF patients with similar LAA morphologies that may have contributed to local thrombogenesis and subsequent embolization.

Case reports

Patient 1

Patient 1 is a 74-year-old man with a history of hypertension, hyperlipidemia, asthma, gastroesophageal reflux disease, and benign prostate hypertrophy (initial CHADS$_2$ score = 1; CHA$_2$DS$_2$-VASc = 2). He had a history of short-lasting (ie, seconds-long) paroxysmal palpitations that had responded to avoidance of caffeinated beverages but had never received a specific rhythm diagnosis. The first

documentation of AF was during the workup of sudden onset weakness in his left lower extremity upon standing from a chair. He denied experiencing accompanying paresthesias, involvement of other extremities, facial weakness, visual disturbance, or alteration in mental status or loss of consciousness. An electrocardiogram (ECG) showed AF.

Results of magnetic resonance imaging (MRI) of the brain revealed a 1-cm ovoid linear focus of T2 hyperintensity, diffusion restriction, and ill-defined enhancement in the right parietal centrum semiovale white matter—findings indicative of a late acute microvascular ischemic infarct.

Carotid duplex images showed no signs of atherosclerotic disease or significant luminal stenosis. The patient was treated with oral anticoagulant (Dabigatran). He presented 6 weeks later with transient symptoms of dysarthria that were diagnosed as a transient ischemic attack despite oral anticoagulation. He was referred to consider strategies for LAA exclusion.

He underwent cardiac computerized tomography (CT) in preparation for a Lariat procedure. The CT results revealed a complex 3-dimensional geometry of the LAA, consisting of a broad, serpentine first lobe with multiple trabeculae, constricting distally at a sharp angle into a thin, linear, and elongated second lobe (Figure 1). LAA inflow velocity was documented at 20 cm/s via transesophageal echocardiography.

Despite the presence of an elongated LAA lobe behind the pulmonary artery, the patient underwent a successful LAA ligation. At 20 months post procedure, he remains thromboembolism-free to date.

Patient 2

Patient 2 is an 86-year-old woman with hypertension, diabetes, coronary artery disease, hyperlipidemia, chronic kidney disease, and hypothyroidism (CHADS$_2$ score = 2; CHA$_2$DS$_2$-VASc = 4). She also has a history of symptomatic sinus bradycardia, for which she had previously undergone implantation of a dual-chamber pacemaker. She had presented 3 years ago with an acute systemic embolism to her left brachial artery, which was associated with chest and left arm pain, paresthesias, arm coldness, and absent pulses in the left brachial, radial, and ulnar arteries. The international normalized ratio at presentation was 1.2. She

was treated with surgical embolectomy. At that point, she was diagnosed with paroxysmal AF based on pacemaker interrogation. She was treated with oral anticoagulation with warfarin. The patient presented 2 years later with weakness and pain in the left lower extremity, resulting in inability to ambulate, cyanosis, and mottling in the left lower extremity and left foot. A CT angiogram demonstrated complete occlusion of the left external iliac artery with a thrombotic embolism. An embolectomy was performed again. At this time, the international normalized ratio was equal to 1. Two

weeks before referral, she sustained a lower gastrointestinal bleed requiring the transfusion of 2 units of packed red blood cells. Pacemaker interrogation revealed sporadic episodes of paroxysmal atrial fibrillation (15% mode-switch). She was referred for consideration of LAA ligation strategies.

A cardiac CT was performed that revealed a wide first lobe bending into a gradually narrowing, linear, and prolonged second lobe (Figure 2). LAA inflow velocity was documented at 26 cm/s via transesophageal echocardiography.

The patient subsequently underwent a successful LAA ligation. She remains thromboembolism-free at 11 months post procedure.

LAA morphology

The shared feature in these patients was the presence of an elongated, narrow LAA lobe that tapered slowly into a pointed tip. This specific anatomy represents a rare variant of the commonly classified chicken wing morphology.[7]

Using the definition of LAA neck area set forth by Beinart et al[11]—as the product of the short and long axes at the point of intersection between the LAA and LA—patient 1's LAA neck long axis measured 1.71 cm, and the short axis measured 1.32 cm (Figure 1). The diameter of the LAA at the point of curvature between its lobes was 1.084 cm. The second elongated lobe spanned 4.1 cm and constricted to a 1.7-mm diameter at its tip. The LAA's depth was 2.21 cm, and the overall LAA volume measured 9.9 cm^3 (Figure 1).

Patient 2's long LAA neck axis measured 2.5 cm, and her short LAA neck axis measured 1.7 cm (Figure 2). The diameter of the LAA at the point of curvature between its lobes was 1.5 cm. The second elongated lobe spanned 5 cm and constricted to a tiny 2.5-mm diameter at its tip. The LAA's depth was 3.26 cm, and the overall LAA volume measured 13.8 cm^3 (Figure 2).

Our patients share an unusually high predisposition to thromboembolic events. This could not have been predicted solely based on their CHADS$_2$ risk factors as their presentation scores were 1 and 2, respectively.

The distinctive feature in both of our patients is the presence of long and narrow appendage lobes. The mechanism of LAA thrombus formation involves local blood stasis.[12] It is conceivable that such stasis could have been particularly severe at the tip of the elongated and narrow appendage lobe.

Multiple studies have attempted to establish morphologic characteristics that increase thromboembolic risk.[7,10,11,13,14] Burrell et al[14] determined the average LAA volume for patients without a prior history of stroke to be 21.7 ± 8.3 cm^3. The mean LAA volume for patients with a history of stroke was 28.8 ± 13.5 cm^3. They established a correlation between LAA volume and stroke risk, indicating that a larger volume could predispose to stroke It appears that neither of our patients exhibits a large LAA volume, with measurements of 9.9 cm^3 for patient 1 and 13.8 cm^3 for patient 2.
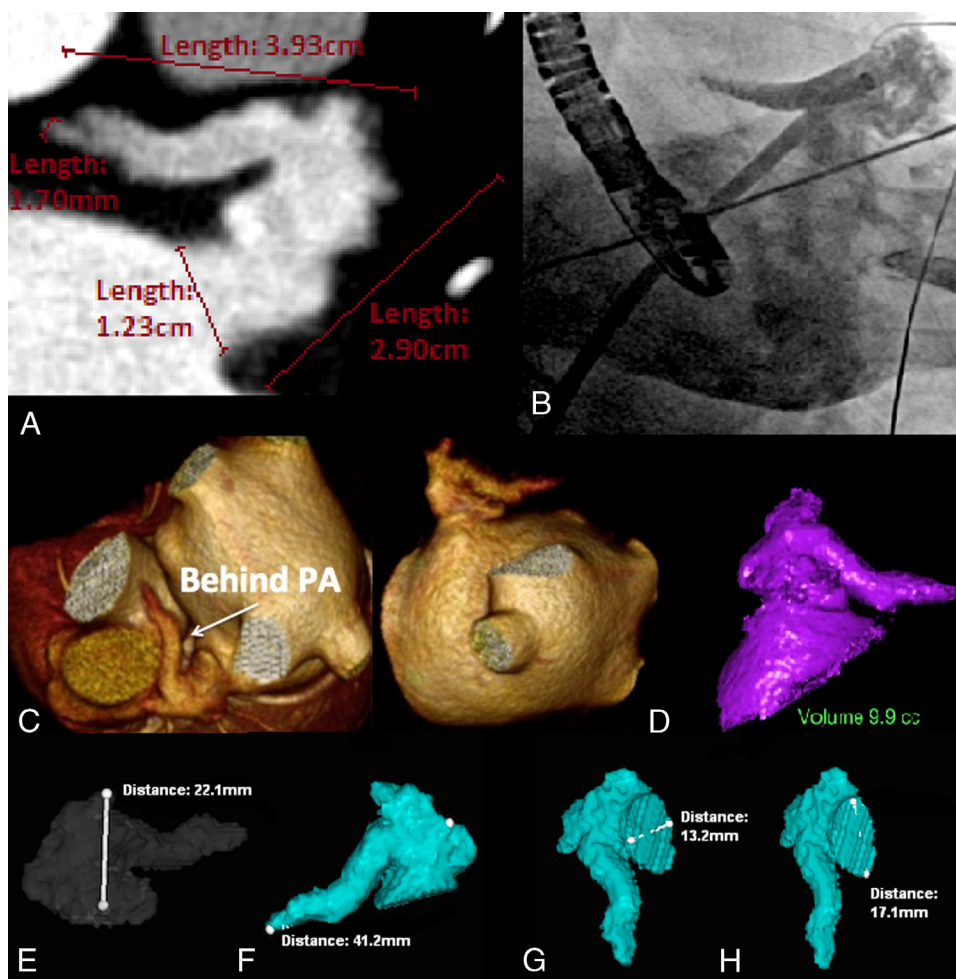
Figure 1   Patient 1 left atrial appendage (LAA) morphology. The LAA exhibits a broad base with few trabeculae superiorly, with a narrow and sharp-angled bend gradually constricting into a thin, elongated lobe. **A:** A computed tomography angiogram showing LAA morphology and anatomy, with lobe length measurements and diameter measurements at multiple points of morphologic significance. **B:** Contrast injection into the LAA delineating its complex anatomy during the ligation procedure. **C:** A 3-dimensional reconstruction of LAA morphology. **D:** LAA volume measurement. **E:** LAA depth. **F:** Second lobe length measurement. **G, H:** Measurements of LAA neck axes.

Beinart et al[11] found both LAA neck dimensions and LAA depth to be independent risk factors for stroke. The study's mean long axis length measured 2.21 ± 0.8 cm, whereas the mean short axis spanned 1.45 ± 0.5 cm. Our patient 1's long axis length was 1.71cm and his short axis spanned 1.32 cm. Similarly, patient 2's long axis spanned 2.54 cm whereas her short axis spanned 1.73 cm. All of these values are comparable to the study's means and should therefore confer no added thromboembolic risk.

Furthermore, the mean LAA depth was established to be 3.3 ± 0.8 cm. Patient 1's LAA depth was 2.2 cm, well below the mean LAA depth from the study. Patient 2's LAA depth measured 3.26 cm, which was comparable to the mean. Once again, these figures indicated no added thromboembolic risk resultant from LAA depth.

Yamamato et al[10] showed that 94.4% of patients with LAA thrombus had ≥3 LAA lobes. The number of LAA lobes was shown to be an independent risk factor for thrombus formation. Both of our patients have 2 LAA lobes and therefore lack this risk factor.

Di Biase et al[7] have proposed a stratification scheme of LAAs based on their morphologies. In their scheme, 4 main morphologies were coined: cactus, windsock, chicken wing, and cauliflower. Patients at low-to-moderate risk with non–chicken wing morphologies were found to be at higher risk of stroke than their chicken wing counterparts. Both of our patients exhibit morphologies best fitted into the chicken wing class, defined as an LAA having an obvious bend in the proximal or middle part of the dominant lobe. This morphologic stratification therefore predicts a lower initial stroke risk for patient 1, but has no bearing on the prognosis of patient 2, who had an initial $CHADS_2$ score of 2.

Anselmino et al[13] studied the impact of LAA morphology on prevalence of silent cerebral ischemia (SCI). Chicken wing, windsock, and cauliflower morphologies were found to relate independently to risk of SCI. Our patients' chicken wing morphology put them at a higher risk of SCI.

Finally, Khurram et al[8] established independent correlations between stroke incidence and both LAA orifice diameter and extent of LAA trabeculation. Patients were
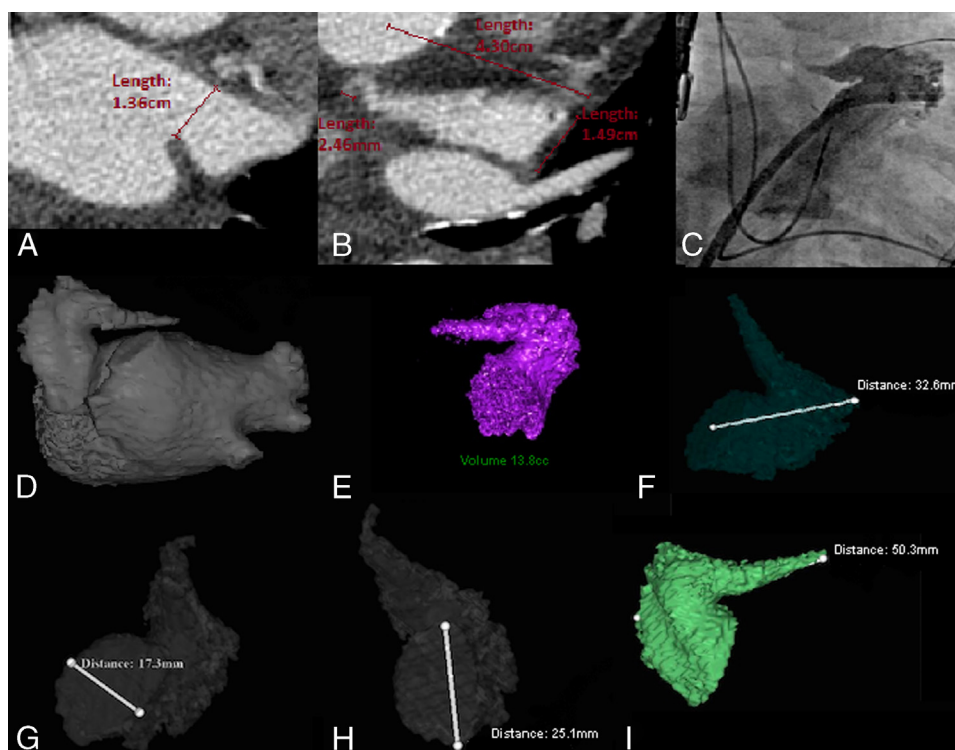
Figure 2 Patient 2 left atrial appendage (LAA) morphology. The LAA exhibits a broad base with few trabeculae superiorly, with a narrow and sharp-angled bend gradually constricting into a thin, elongated lobe. **A, B:** Computed tomography angiograms showing LAA morphology with measurements of length of the second lobe and the diameter at the point of curvature and second lobe tip. **C:** Contrast injection into the LAA delineating its complex morphology during the ligation procedure. **D:** A 3-dimensional reconstruction of LAA morphology. **E:** LAA volume measurement. **F:** LAA depth. **G, H:** Measurements of LAA neck axes. **I:** Second lobe length measurement.

stratified into mild, moderate, and extensive trabeculation groups. Extensive trabeculae were independently associated with stroke risk. Neither of our patients exhibited extensive trabeculation of the LAA wall, however, making this risk factor noncontributory to their thromboembolic history. The study also found that shorter LAA orifice diameters were associated with higher stroke risk. Mean diameter was 2.26 ± 0.52 cm in case subjects with a history of transient ischemic attack or stroke vs 2.78 ± 0.71 cm in controls. Our patients' LAA orifice diameters measured 1.71 cm and 2.51 cm respectively, so orifice diameter was a possible contributing factor for patient 1's thromboembolic history.

Overall, it appears that both of our patients' morphologic characteristics should place them in a relatively safe zone for thromboembolic risk. They lack risk factors in LAA volume, neck axis lengths, LAA depth, number of LAA lobes, extent of trabeculation, and overall morphologic stratification. Nonetheless, we postulate that their common LAA anatomy has predisposed them to recurrent thromboembolism. The presence of a substantially sized, thin, and elongated second lobe appears to augment blood stasis and consequent thrombus formation. This same reasoning is presented by Kosiuk et al[15] in explaining increased periprocedural thromboembolism following AF ablation in patients with chicken wing morphology.

Current morphologic classification schemes based on stroke epidemiology may help guide treatment plans, but they fail to do so predictably and infallibly. A deeper understanding of the effect of LAA anatomy on blood flow and thrombus formation may provide a more reliable morphology-based risk estimation scheme.

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