

Left Atrial Appendage Characteristics Assessed with Cardiac Computed Tomography in Patients with Atrial Fibrillation and Severe Mitral Valve Disease

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Purpose: The morphological and functional characteristics and clinical significance of the left atrial appendage (LAA) are well established in patients with non-valvular atrial fibrillation (AF). However, data on the LAA characteristics in patients with mitral valve (MV) disease are limited. This study aimed to identify the LAA characteristics in AF patients with severe MV disease.

Materials and Methods: A total of 506 AF patients who underwent cardiac computed tomography (CT) as preoperative evaluations for MV surgery were retrospectively analyzed. The prevalences of different LAA morphologies (cactus, cauliflower, wind-sock, chicken wing), LAA ostium diameter, LAA volume, and LAA flow stasis or thrombus were assessed. The LAA variables were compared according to the predominant MV dysfunction.

Results: The most common LAA morphology was cactus (n=211, 41.7%), followed by cauliflower (n=143, 28.3%), windsock (n=90, 17.8%), and chicken wing (n=60, 11.9%). The average LAA ostium maximal diameter and LAA volume were 35.3±8.0 mm and 22.1±15.1 mL, respectively. LAA stasis was found in 215 patients (42.5%) and LAA thrombus in 93 patients (18.4%). Patients with mitral stenosis predominance showed significantly smaller LAA volume compared to those with mitral regurgitation predominance (17.8±11.7 mL vs. 26.9±16.8 mL, $p<0.001$). However, LAA flow stasis [190 (71.7%) vs. 25 (10.4%), $p<0.001$] and thrombus [89 (33.6%) vs. 4 (1.7%), $p<0.001$] were remarkably prevalent in these patients.

Conclusion: Due to advanced LAA remodeling in AF patients with severe MV disease, the morphologic distribution of LAA types differs from that established in patients without MV disease.

Key Words: Left atrial appendage, mitral valve disease, atrial fibrillation, computed tomography

Received: December 31, 2024 **Revised:** March 6, 2025

Accepted: March 20, 2025 **Published online:** June 10, 2025

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•The authors have no potential conflicts of interest to disclose.

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INTRODUCTION

The left atrial appendage (LAA) is a pouch-like projection from the main body of the left atrium (LA) that is highly prone to stasis and thrombus formation during atrial fibrillation (AF). AF is responsible for the majority of embolic strokes.^{1,2} There has been growing interest in LAA anatomy and function due to advancements in technology that allow for the exclusion of the LAA from systemic circulation through surgical or interventional methods.³⁻⁶ A few studies have demonstrated morphological and functional characteristics of LAA and their clinical significance in AF patients without significant mitral valve (MV) disease.^{5,7,8} However, detailed information about LAA

shape, size, and function in patients with severe MV disease is lacking, although patients with severe MV disease are more likely to have AF due to chronic pressure or volume overload on the LA and are at greater risk of stroke or systemic embolism.^{9,10}

In clinical practice, there are no clear standard guidelines on which patients should undergo LAA surgery when performing MV surgery; therefore, concomitant LAA surgery is generally determined depending on the patient's clinical risk of surgery and surgeon preference rather than the characteristics of the LAA itself. In some cases, residual cardiovascular risk due to LAA may occur after MV surgery. Conversely, surgical risk may increase as LAA surgery is added. Therefore, there is a need for image-based risk stratification to identify patients who require LAA surgery among patients preparing to undergo MV surgery.

In this study, we aimed to investigate the structural and functional characteristics of LAA by cardiac computed tomography (CT) in AF patients with severe MV disease. We also compared the characteristics of LAA between mitral stenosis (MS)-dominant and mitral regurgitation (MR)-dominant patients.

MATERIALS AND METHODS

Study population

A total of 972 patients who underwent transthoracic echocardiography and cardiac CT for preoperative evaluation were retrospectively identified at a single tertiary center (Severance Cardiovascular Hospital, Seoul, Republic of Korea) between January 2006 and July 2019. Patients with sinus rhythm ($n=455$), history of LAA surgery ($n=6$), and unmeasurable LAA ("auto-obiterated," $n=5$) were excluded. As a result, 506 patients were finally studied. We compared LAA structural and functional characteristics among groups stratified by the predominant MV dysfunction before MV surgery [predominant MS ($n=265$) vs. predominant MR ($n=241$)]. Fig. 1 shows a schematic study flowchart. This study was approved by the Institutional Review Board of

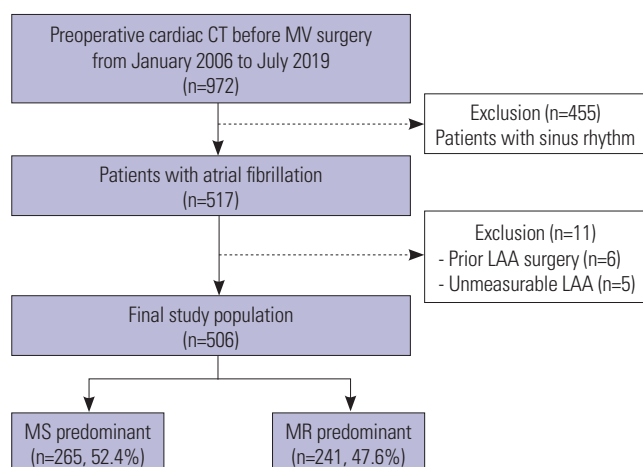


Fig. 1. Flowchart of this study. CT, computed tomography; MV, mitral valve; LAA, left atrial appendage; MS, mitral stenosis; MR, mitral regurgitation.

the Yonsei University Health System (approval number: 2021-0510-003) and complied with the Declaration of Helsinki. The requirement for informed consent was waived since this was a retrospective study, and the data were analyzed anonymously.

Echocardiography

Standard two-dimensional and Doppler echocardiography measurements were conducted following the American Society of Echocardiography guidelines.¹¹ The left atrial volume index was measured using a modified Simpson's method with apical 4- and 2-chamber views and indexed based on body surface area. Right ventricular systolic pressure was estimated by summing the peak systolic pressure from the maximal tricuspid regurgitation (TR) jet velocity using a modified Bernoulli's equation, and right atrial pressure was estimated using the diameter and collapsibility of the inferior vena cava. The severities of MS, MR, and TR were assessed under the current guidelines.^{12,13} Significant valvular dysfunction was defined inclusively as moderate or severe grades of dysfunction. MS predominance was defined as significant MS, and MR predominance was defined as only significant MR without significant MS.

Cardiac CT

The indication for CT was to evaluate valvular function, coronary patency, and adjacent thoracic structures at the clinician's discretion.

Cardiac CT scanning protocol, generation of the three-dimensional (3D) rendering, and data extraction were all conducted following conventional guidelines. Cardiac CT scans were performed with a dual-source CT scanner (SOMATOM Definition Flash or Force; Siemens Healthcare, Erlangen, Germany), a 64-slice multidetector CT (SOMATOM Sensation 64; Siemens Medical Solution, Erlangen, Germany), or wide-coverage 256-row CT (Revolution CT; GE Healthcare, Waukesha, WI, USA). They were performed with retrospective electrocardiographically gated data acquisition (0%–90% phase) on spiral mode and with the prospective gated acquisition with a padding range of 20% to 120% of the R-R interval on axial mode. All CT scans were performed using the triple-phase contrast injection method (70 mL of iopamidol followed by 30 mL of 50% blended iopamidol with saline and 20 mL of saline at 5 mL/s). For all patients, 10 datasets were reconstructed at 10% intervals of the cardiac cycle, and the images were analyzed using dedicated 3D software (Aquaris iNtuition, Ver 4.4.1, TeraRecon, San Mateo, CA, USA).

LAA morphology was evaluated and classified by one expert radiologist (Y. J, K) who was blinded to the clinical data. The LAA morphologies were classified into four types (cactus, cauliflower, windsock, chicken wing), as previously described (Fig. 2A).^{5,14} The cactus type has a dominant central lobe, one or more secondary lobes, and a total length <4 cm. The cauliflower type is characterized by a length <4 cm and complex inter-

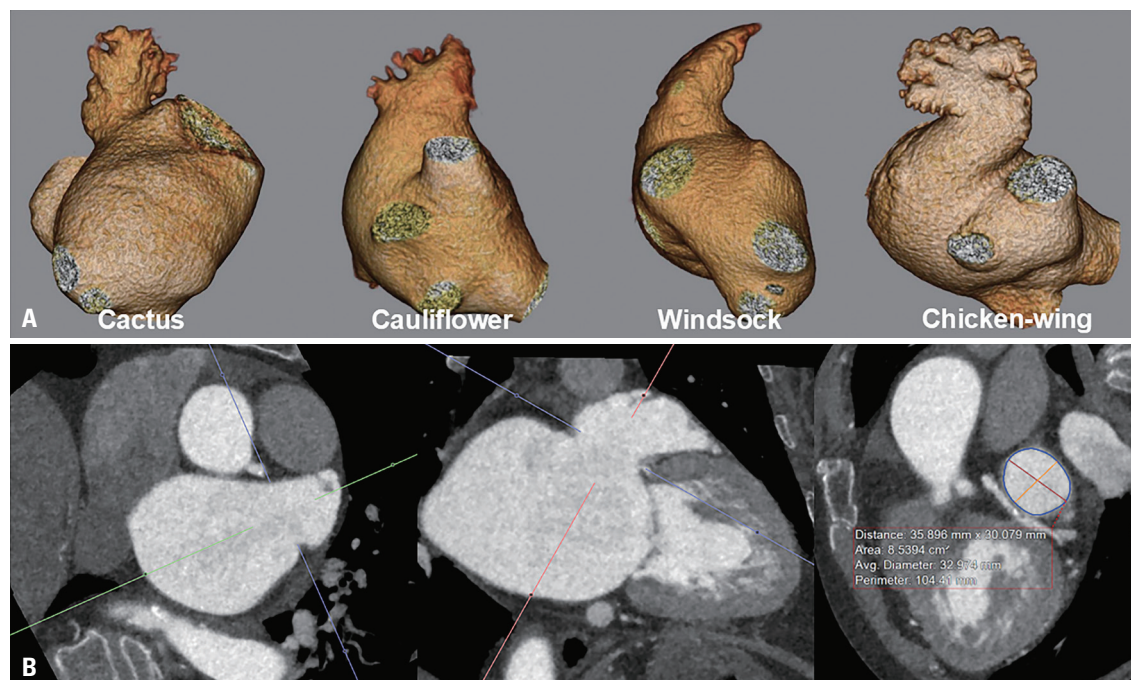


Fig. 2. Assessment of left atrial appendage by cardiac computed tomography shape (A) and size (B).

nal structures. The windsock type presents with one dominant lobe and several secondary or even tertiary lobes, a length >4 cm, and a bend angle $>100^\circ$. The chicken wing type consists of only one lobe, a length >4 cm, and a bend angle $<100^\circ$.¹⁴

The LAA orifice was defined as the plane connecting the superior pulmonary vein ridge to the inferior junction of the LA/LAA at the circumflex artery. Maximal, minimal, and average diameters, as well as the perimeter and area of LAA orifice, were measured (Fig. 2B). LAA thrombus was identified as the presence of contrast filling defects in both early and delayed phase images, while LAA stasis was defined by contrast filling defects appearing in early images but disappearing in delayed images.¹⁵ The LA was semiautomatically segmented on end-systolic phase images, and the pulmonary veins were excluded. In cases of stasis or thrombus in LAA, manual correction was applied to measure LAA volume.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation, and categorical variables are presented as frequency and percentage. Baseline clinical and echocardiographic characteristics of patients were analyzed using Student's t-test for continuous variables and chi-squared (χ^2) test for categorical variables. All tests were two-sided, and statistical significance was defined as $p < 0.05$. All statistical analyses were performed using R statistical software (version 4.0.0; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics

Table 1 shows the baseline clinical characteristics of the study population. The average age of 506 patients was 61.3 ± 11.0 years, and 325 (64.2%) were female. All patients had AF, and 45.1% had been diagnosed with hypertension and 19.4% with diabetes mellitus. A total of 20.2% of patients had experienced previous stroke, and 96.2% were treated with anticoagulants before MV surgery. In the study population, MV disease of rheumatic etiology was found in 62.1%, and MS and MR predominance were 265 (52.4%) and 241 (47.6%), respectively. Of the patients with MR predominance, 196 had primary MR and 45 had secondary MR (atrial functional MR=25 patients). The average LA volume index was high at 112.4 ± 79.1 mL/m², the estimated pulmonary artery systolic pressure was as high as 44.7 ± 15.9 mm Hg, and significant TR was observed in 221 (43.7%) patients. In terms of surgical characteristics, mechanical MV replacement was performed in about half of the patients, and maze operation was performed in 274 (54.2%) patients. Of the 262 (51.8%) patients who underwent LAA surgery, 210 underwent LAA obliteration and 52 underwent LAA resection.

LAA characteristics on cardiac CT

Table 2 demonstrates the characteristics of LA and LAA on cardiac CT. Among LAA shapes, cactus ($n=211$, 41.7%) was the most common, followed by cauliflower ($n=143$, 28.3%), windsock ($n=90$, 17.8%), and chicken wing ($n=60$, 11.9%). There were two patients who could not be classified into any of the four shapes, and one patient had a cone-shaped LAA, showing

Table 1. Baseline Characteristics of the Study Population (n=506)

	Value
Demographic and clinical characteristics	
Age at operation, yr	61.3±11.0
Female sex	325 (64.2)
Body mass index, kg/m ²	23.0±3.1
Hypertension	228 (45.1)
Diabetes mellitus	98 (19.4)
Prior history of stroke	102 (20.2)
Dyslipidemia	141 (27.9)
Coronary artery disease	46 (9.1)
Chronic kidney disease	33 (6.5)
Preoperative anticoagulant use	487 (96.2)
Preoperative antiplatelet use	56 (11.1)
Echocardiographic characteristics	
Rheumatic MV disease	314 (62.1)
MS predominance	265 (52.4)
MR predominance	241 (47.6)
LV ejection fraction, %	60.3±10.6
LA volume index, mL/m ²	112.4±79.1
Estimated PASP, mm Hg	44.7±15.9
Significant TR ≥ moderate	221 (43.7)
Surgical characteristics	
MVR (mechanical)	252 (49.8)
MVR (bioprosthetic)	92 (18.2)
MV repair	162 (32.0)
Maze operation	274 (54.2)
Concomitant surgery	411 (81.2)
Aortic valve surgery	145 (28.7)
Tricuspid valve surgery	352 (69.6)
Coronary artery bypass surgery	13 (2.6)
LAA surgery	262 (51.8)
LAA obliteration	210 (41.5)
LAA resection	52 (10.3)

MV, mitral valve; MS, mitral stenosis; MR, mitral regurgitation; LV, left ventricle; LA, left atrium; PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation; MVR, mitral valve replacement; LAA, left atrial appendage. Data are presented as mean±standard deviation or n (%).

progressive reduction in dimension from the orifice to the distal tip. The average maximal and minimal diameters of LAA ostium were 35.3±8.0 mm and 27.4±6.7 mm, respectively, and the average diameter was 31.1±7.1 mm. The average perimeter of the LAA ostium was 99.5±22.5 mm and the area was 8.0±3.9 cm². The LA volume measured by CT was increased to 328.5±180.1 mL, and the LAA volume was also increased to 22.1±15.1 mL. LAA stasis was found in 215 patients (42.5%) and LAA thrombus were in 93 patients (18.4%). The proportion of thrombus or flow stasis in the LAA varied by the shape of the LAA, as shown in Supplementary Table 1 (only online). LAA thrombus was the most common in the windsock shape, followed by the cauliflower shape and cactus shape, while it was significantly less common in the chicken wing shape. Flow stasis was most fre-

Table 2. Characteristics of LA and LAA on Cardiac CT (n=506)

	Value
LAA shape	
Cactus	211 (41.7)
Cauliflower	143 (28.3)
Windsock	90 (17.8)
Chicken wing	60 (11.9)
Others	2 (0.8)
LAA and LA size	
LAA ostium maximal diameter, mm	35.3±8.0
LAA ostium minimal diameter, mm	27.4±6.7
LAA ostium average diameter, mm	31.1±7.1
LAA ostium perimeter, mm	99.5±22.5
LAA ostium area, cm ²	8.0±3.9
LA volume, mL	328.5±180.1
LA volume index, mL/m ²	193.5±110.4
LAA volume, mL	22.1±15.1
LAA volume index, mL/m ²	13.1±9.1
LAA stasis or thrombus	
LAA flow stasis	215 (42.5)
LAA thrombus	93 (18.4)

LAA, left atrial appendage; LA, left atrium.

Data are presented as mean±standard deviation or n (%).

quent in the cauliflower shape, followed by windsock and cactus shapes, while it was rarely seen in the chicken wing shape.

Comparison of LAA characteristics according to MV dysfunction

Table 3 shows the characteristics of 265 patients with MS predominance and 241 patients with MR predominance. In MS-predominant patients, the cactus type (n=103, 38.9%) was the most common, followed closely by the cauliflower type (n=97, 36.6%), whereas in patients with MR predominance, the cactus type (n=108, 44.8%) was overwhelmingly prevalent. In MS-predominant patients, the chicken wing type was particularly low in prevalence, but in MR predominance, cauliflower, windsock, and chicken wing all showed similar prevalence rates. Both LAA and LA measured values MS-predominant patients were significantly smaller than those of MR-predominant patients. However, LAA stasis (n=190, 71.7%) and thrombus (n=89, 33.6%) were considerably more common in patients with MS predominance (Fig. 3). Overall, the relationship between LA volume and LAA volume demonstrated a significant linear correlation ($r=0.452$, $p<0.001$). Significantly, larger LAA volumes were associated with larger LA volumes. Notably, this linear correlation was stronger in the MR-predominant group compared to the MS-predominant group (Fig. 4).

DISCUSSION

The principal findings of the present study were as follows. First,

Table 3. Characteristics of Groups Stratified by Mitral Valve Dysfunction

	MS predominance (n=265)	MR predominance (n=241)	p
Echocardiographic characteristics			
LV ejection fraction, %	59.2±10.3	61.5±10.8	0.017
LA volume index, mL/m ²	111.8±93.1	113.0±60.3	0.863
Estimated PASP, mm Hg	44.6±16.2	44.8±15.6	0.864
Significant TR≥moderate	106 (40.0)	115 (47.7)	0.097
CT characteristics			
LAA shape			<0.001
Cactus	103 (38.9)	108 (44.8)	
Cauliflower	97 (36.6)	46 (19.1)	
Windsock	45 (17.0)	45 (18.7)	
Chicken wing	18 (6.8)	42 (17.4)	
Other	2 (0.8)	0 (0.0)	
LAA and LA size			
LAA ostium maximal diameter, mm	33.4±7.5	37.4±8.1	<0.001
LAA ostium minimal diameter, mm	26.0±6.1	28.9±6.9	<0.001
LAA ostium average diameter, mm	29.4±6.5	32.8±7.2	<0.001
LAA ostium perimeter, mm	94.2±20.7	105.3±23.0	<0.001
LAA ostium area, cm ²	7.1±3.2	8.9±4.3	<0.001
LA volume, mL	313.1±186.1	345.4±172.0	0.044
LA volume index, mL/m ²	184.9±114.5	202.9±105.2	0.067
LAA volume, mL	17.8±11.7	26.9±16.8	<0.001
LAA volume index, mL/m ²	10.6±6.9	15.8±10.3	<0.001
LAA stasis or thrombus			
LAA flow stasis	190 (71.7)	25 (10.4)	<0.001
LAA thrombus	89 (33.6)	4 (1.7)	<0.001

MS, mitral stenosis; MR, mitral regurgitation; LV, left ventricle; LA, left atrium, PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation; CT, computed tomography; LAA, left atrial appendage; LA, left atrial.

Data are presented as mean±standard deviation or n (%).

the distributions of LAA shape and LAA size in AF patients with severe MV disease were different from those previously recognized in AF patients without MV disease probably associated with advanced LAA remodeling. The most common LAA morphology was the cactus type, followed by cauliflower. Second, flow stasis and thrombus were more common in MS-predominant patients, despite the fact that LAA volume was higher in patients with MR predominance.

The LAA is a remnant of the embryonic LA, located in the left atrioventricular groove and in close proximity to the left circumflex artery, left superior pulmonary vein, MV annulus, and left phrenic nerve.¹⁶ The characteristics of the LAA are well established in patients with non-valvular AF.^{5,7,8,17} A previous study demonstrated that the LAA ostium typically has an oval shape (68.9%), with a maximum depth between 16 mm and 51 mm and a long diameter between 10 mm and 40 mm. In only

5.7% of cases, the form is circular.¹⁷ A prior CT-based study characterized LAA morphology into four types.⁸ A chicken wing appearance with bending in the LAA was the most common at 48% of the total, followed by a cactus with a dominant central lobe and secondary lobes that extend from the central lobe in both superior and inferior directions.⁸ The windsock appearance with a single dominant lobe accounted for 19%, and the cauliflower with a short overall length and complex internal structures comprised 3%.⁸

However, since the LAA is a dynamic structure with volume and size that vary depending on loading conditions, information for LAA structure in AF patients without significant valve dysfunction is limited in value for reflecting advanced LA and LAA remodeling caused by significant MV dysfunction.¹⁸⁻²⁰ MS is related to LA dilation in response to pressure overload caused by fibrosis and/or calcification of the LA,¹⁹ resulting in LAA dysfunction, reduced LAA flow velocities, and an elevated risk of thrombus.^{19,21} However, in chronic severe MR, the main pathophysiology of LA and LAA remodeling is due to chronic volume overload.^{19,22} In AF patients with severe MV disease, valve hemodynamic factors affect LAA structure and function and must be considered. However, comprehensive imaging studies are lacking and such factors remain unexplored. In cases of severe MV disease, the distribution of LAA morphology was different from what was previously established regarding AF patients without significant MV disease, and the size of the LAA ostium was significantly larger. Therefore, the results of this study using CT have high clinical value by demonstrating structural and functional differences in the LAA among AF patients with MV disease. Additionally, differences in the LAA structure and function between MS-predominant and MR-predominant patients suggest that stroke risk varies depending on the underlying disease.

The role of surgical LAA occlusion during cardiac surgery in preventing potential thromboembolism has been a hot topic of discussion over the past few decades.²³⁻²⁵ A number of recent meta-analyses on the outcomes of surgical LAA occlusion during cardiac surgery have indicated that surgical LAA occlusion is an effective treatment option for preventing future thromboembolism and stroke in patients with AF.^{24,26,27} Furthermore, the LAAOS III trial found that among participants with AF who had undergone cardiac surgery, those who had concomitant LAA occlusion experienced a lower risk of ischemic stroke or systemic embolism compared to those without it.²⁴ While these studies highlight the benefits of surgical LAA occlusion, there are also conflicting results and concerns. A study from a large retrospective cohort in the United States has shown that concomitant surgical LAA occlusion during isolated coronary artery bypass graft surgery in patients with AF was associated with higher likelihood of 30-day readmission along with an increased risk of postoperative respiratory failure and acute kidney injury.²⁵ LAA has key neuroendocrine and hemodynamic functions by producing atrial natriuretic peptides and is also a

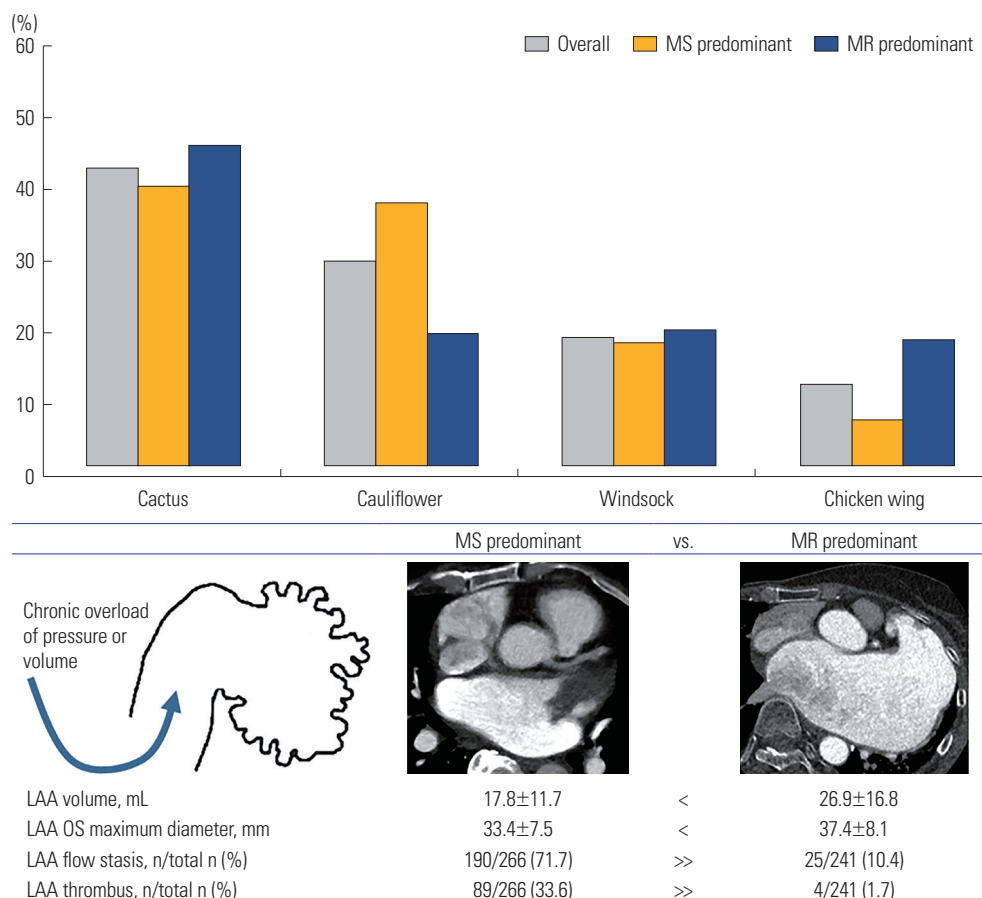


Fig. 3. Comparisons of LAA characteristics in groups stratified by mitral valve dysfunction. MS, mitral stenosis; MR, mitral regurgitation; LAA, left atrial appendage; OS, ostial.

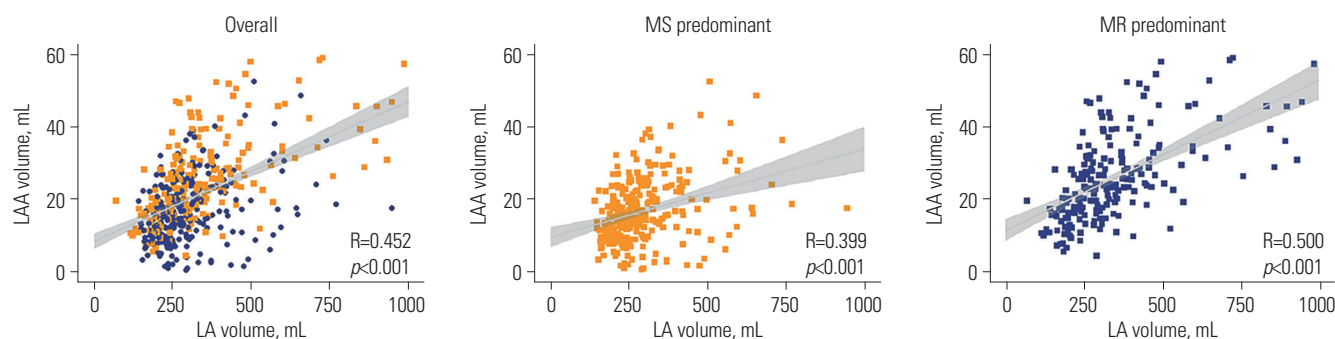


Fig. 4. Correlations between LA and LAA volume in groups stratified by mitral valve dysfunction. MS, mitral stenosis; MR, mitral regurgitation; LAA, left atrial appendage; LA, left atrial.

reservoir of cardiac progenitor cells.²⁸ Therefore, epicardial LAA excision results in decreased serum levels of atrial natriuretic peptide and noradrenaline.²⁹ In addition, incomplete LAA occlusion (such as residual appendage stump or gap) commonly occurs and may be another risk factor for thromboembolic events.³⁰ Concerns remain regarding surgical LAA occlusion during MV surgery, including potential decreases in LA function combined with maze operations, bleeding complications from additional LAA surgery, and the risk of paravalvular leakage of the mitral prosthesis due to tissue shortage.^{29,31,32} There-

fore, LAA preservation during cardiac surgery in patients with AF also needs to be applied on an individualized basis.

When patients with AF undergo cardiac surgery, concomitant surgical LAA occlusion or exclusion is recommended as class IIb in the 2016 European Society of Cardiology Guidelines,³³ and as class IIa in the European Society of Thoracic Surgeons 2017 clinical practice guidelines.³⁴ However, the recently announced 2023 ACC/AHA/HCCP/HRS guidelines for AF management recommends Class I, Level of Evidence A for surgical occlusion or exclusion of the LAA during concomitant cardiac

surgery in patients with a CHA2DS2-VASc score ≥ 2 or equivalent stroke risk, in addition to continued anti-coagulation.³⁵ However, none of the three guidelines provide a substantiating image-based standard for considering concomitant LAA surgery. Additionally, considering the possibility of LA and LAA reverse remodeling or conversion of AF to sinus rhythm after MV surgery, more evidence is required from patients who undergo MV surgery.

To our knowledge, this is the first study to include a detailed structural evaluation of the LAA in AF patients with severe MV disease. In this study, which included approximately equal numbers of MS and MR patients, the average maximal LAA ostium diameters of MS and MR patients were 33.4 ± 7.5 mm and 37.9 ± 8.3 mm, respectively. This average size is what makes percutaneous LAA occlusion using commercially available devices challenging. Therefore, when conducting MV surgery, it is important to determine whether to perform concomitant LAA surgery. Contrary to a previous report which identified the chicken-wing shape as most common, patients with severe MV disease were more often classified as cactus or cauliflower types. In addition, when analyzing CT images, there were patients in whom the LAA and LA appeared to have a common chamber shape, perhaps due to advanced LA and LAA remodeling. In such cases, the boundary between the LA and LAA was ambiguous, complicating surgical LAA occlusion or exclusion. To improve the efficacy and safety of LAA surgery, there is a need for more and improved imaging-based evidence.

This study had a few limitations. First, only patients who had AF and underwent mitral surgery with no complications were included. Second, this study was conducted at a single tertiary center by comprehensively reviewing retrospective and prospective data. Therefore, selection and referral bias were possible, as well as unobserved confounding factors. Third, we were unable to analyze the clinical outcomes or sustained occlusion to compare the group that underwent concomitant LAA surgery and the group that did not. Further research will be needed to identify factors and clinical outcomes associated with performing concomitant LAA surgery. Fourth, as the analysis was mainly performed through CT, the implementation of functional assessments, such as LA or LAA strain, was limited. Fifth, since all study subjects were of East Asian ancestry, it may be difficult to generalize our results to other populations or regions.

In conclusion, the distribution of LAA shapes in patients with severe MV disease was quite different from those previously documented, particularly when examining patients with advanced remodeling of LA and LAA. LAA was greater in MR patients than in MS patients, and flow stasis and thrombus were more common in MS patients.

ACKNOWLEDGEMENTS

This study was supported by faculty research grants of Yonsei

University College of Medicine (6-2021-0096, 6-2024-0110).

AUTHOR CONTRIBUTIONS

Conceptualization: Chi Young Shim. **Data curation:** Hee Jeong Lee, Jiwon Seo, Young Jin Kim, and Chi Young Shim. **Formal analysis:** Hee Jeong Lee and Jiwon Seo. **Funding acquisition:** Chi Young Shim. **Investigation:** Hee Jeong Lee and Jiwon Seo. **Methodology:** Kyu Kim, Young Joo Suh, Young Jin Kim, and Chi Young Shim. **Project administration:** Young Jin Kim and Chi Young Shim. **Resources:** Seo-Yeon Gwak, Iksung Cho, and Geu-Ru Hong. **Software:** Young Jin Kim and Chi Young Shim. **Supervision:** Seung-Hyun Lee, Sak Lee, Geu-Ru Hong, Jong-Won Ha, Young Jin Kim, and Chi Young Shim. **Validation:** Young Joo Suh, Young Jin Kim, and Chi Young Shim. **Visualization:** Young Jin Kim and Chi Young Shim. **Writing-original draft:** Hee Jeong Lee and Jiwon Seo. **Writing-review & editing:** Young Jin Kim and Chi Young Shim. **Approval of final manuscript:** all authors.

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