Received: 24 October 2022 | Accepted: 15 November 2022
DOI: 10.1111/anec.13027

ORIGINAL ARTICLE

WILEY

# Study on the correlation between false-positive filling defect in LAA CT and LAA structure in patients with atrial fibrillation based on TEE

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## Abstract

**Objective:** This study aims to explore the actual meaning of "false positive filling defect" in left atrial appendage (LAA) computed tomography (CT) in patients with atrial fibrillation (AF), with transesophageal echocardiography (TEE) as the gold standard.

**Methods:** Patients with AF undergoing cardiac CT angiography and TEE examinations for proposed radiofrequency catheter ablation between October 2020 and October 2021 were selected as the study subjects. Transesophageal echocardiography was taken as the "gold standard," and spontaneous echocardiographic contrast (SEC) and thrombus events were defined as positive events. The CT manifestations were classified into three groups (true positive, false positive, and true negative) to evaluate the differences in left atrium (LA) anterior–posterior diameter (LAAP), LA anterior wall thickness, and LAA orifice long diameter and short diameter, area, and depth between the three groups.

**Results:** (1) There was no statistical difference in LA anterior wall thickness between the three groups ($p > .05$); there was a statistical difference in LAAP (only) between the true-positive group and the true-negative group ($p < .05$). (2) There was a statistical difference in LAA orifice long diameter, short diameter, and area between the true-positive group and the true-negative group as well as between the false-positive group and the true-negative group ($p < .05$). (3) There was a statistical difference in LAA depth between the true-positive group and the false-positive group as well as between the true-positive group and the true-negative group ($p < .05$). (4) The area under the receiver operator characteristic curve (AUC) of LAA depth affecting the LAA thrombus and SEC was 0.863 (confidence interval = 0.718–1.000), the sensitivity was 77.8%, and the specificity was 90.6% for predicting the occurrence of LAA thrombus and SEC in patients with nonvalvular AF (NVAF) and an LAA depth of ≥50.84 mm.

**Conclusions:** There was a difference in LAA diameter between the TEE-based CT false-positive group and the other groups. A "CT false positive" is an objectively existing state, and CT might be able to identify the LAA hemodynamic disorder earlier than

TEE. Furthermore, a CT+TEE combined application could more accurately evaluate LAA hemodynamics in patients with AF.

**KEYWORDS**

atrial fibrillation, cardiac CTA, left atrial appendage thrombus/spontaneous echocardiographic contrast, transesophageal echocardiography

## 1 | INTRODUCTION

Atrial fibrillation (AF) is one of the most common types of clinical arrhythmia. Patients with AF are prone to thrombosis in the left atrial appendage (LAA), which can be leading to severe thromboembolism. This has attracted close concern in clinical practice. Currently, radiofrequency catheter ablation (RFCA) has become a radical surgery for patients with AF, and thrombosis in LAA is an absolute contraindication of RFCA (Hindricks et al., 2021). Spontaneous echocardiographic contrast (SEC) represents blood flow stasis and the state before thrombosis (Wang et al., 2000); studies have demonstrated that LAA SEC in patients with AF has an equally important clinical significance as thrombus (Guo et al., 2022; Kosmalska et al., 2022).

Transesophageal echocardiography (TEE) is the gold standard for examination of LAA thrombus and SEC (He et al., 2017; Kobza et al., 2013); however, there are many contraindications, and severe complications may be caused during the examination. The accuracy of examination results is chiefly dependent on the experience of the operator, and TEE is an invasive examination that cannot accurately evaluate the anatomic relationship between the pulmonary vein and the LA.

Currently, multislice spiral computed tomography (CT) angiography (CTA) has become a routine examination for patients with AF before RFCA; it aims to objectively and spatially display the anatomic relationship between the left atrium (LA) and the pulmonary vein as well as accurately measure data related to the pulmonary vein, LA, and LAA due to its high temporal and spatial resolution, facilitating individualized treatment with RFCA based on patient anatomic variation. Studies have also demonstrated multislice spiral CTA's significant application value in the detection of LAA thrombus and SEC (He et al., 2017, 2020; Liu et al., 2017; Romero et al., 2013; Xing et al., 2017); this is particularly due to its extremely high negative predictive values (Guo et al., 2022; He et al., 2017; Tian et al., 2020; Yu et al., 2021). However, some patients with false-positive results were found in daily operations. At present, there is no definite explanation for such false-positive results in the literature. In this study, TEE was taken as the gold standard, and the clinical significance of CT false-positive results was explored, with detected thrombus and/or SEC as positive events.

## 2 | MATERIALS AND METHODS

### 2.1 | General data

A total of 86 patients with AF undergoing cardiac CTA and TEE examinations for proposed RFCA in Cangzhou Central Hospital between October 2020 and October 2021 were consecutively selected as the study subjects. All patients signed an informed consent form before examination. Exclusion criteria: (1) Patients with an interval of >2 days between the contrast-enhanced CT scan and TEE; (2) patients with poor CT imaging quality that did not meet the measuring requirements; (3) patients with a combination of AF and cardiac diseases affecting the examination results; and (4) patients with stenosis, esophageal varices, deformities, and other esophageal diseases affecting the examination results.

Case groups: (1) True-positive group: The CT showed a filling defect, and the TEE showed a positive result (Figures 1 and 2); (2) false-positive group: The CT showed a filling defect, and the TEE showed a negative result (Figure 3); (3) true-negative group: The CT showed no filling defect, and the TEE showed a negative result (Figure 4); (4) false-negative group: The CT showed no filling defect, and the TEE showed a positive result. The CT has an extremely high negative predictive value in the detection of LAA thrombus and SEC (Guo et al., 2022; He et al., 2017; Tian et al., 2020; Yu et al., 2021), and only one CT false-negative case occurred in this study; hence, the false-negative result was not included in the statistics.

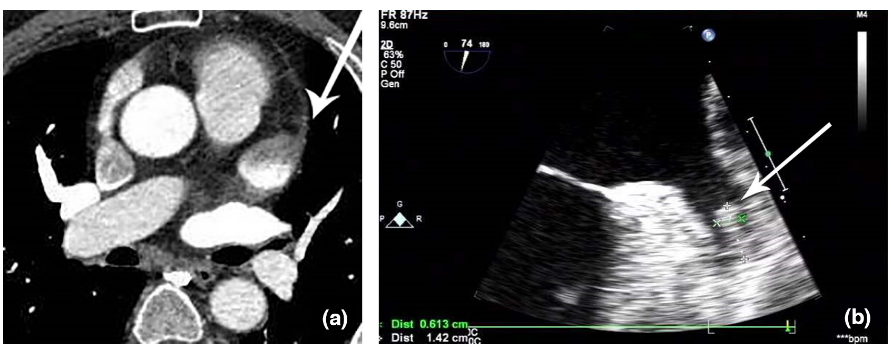


FIGURE 1 True-positive group (thrombus). (a) CT findings: Contrast agent filling defect in LAA (indicated by arrow); (b) TEE findings: A thrombus sized 14.2×6.13 mm at LAA tip (indicated by arrow).

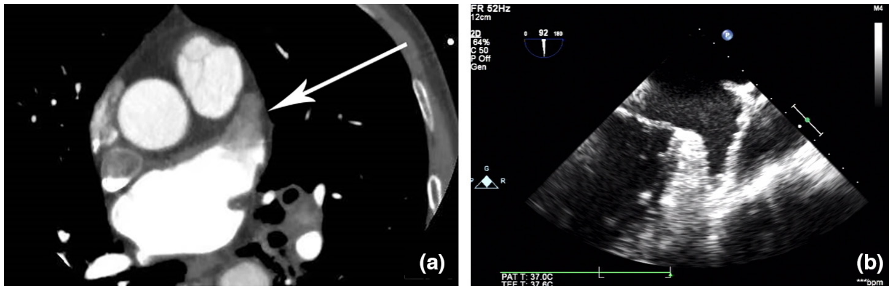


**FIGURE 2** True-positive group (SEC). (a) CT findings: Contrast agent filling defect in LAA (indicated by arrow); (b) TEE findings: SEC in LA and LAA.

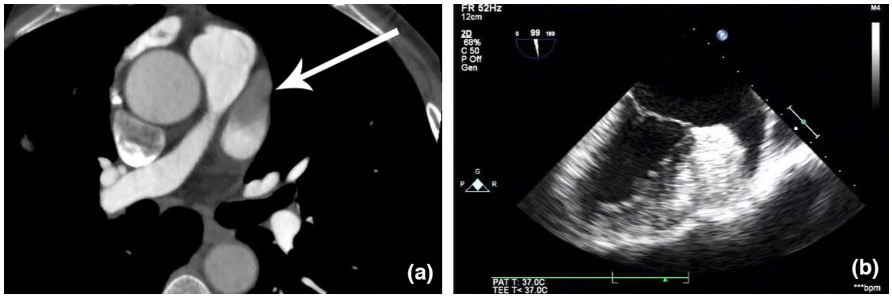


**FIGURE 3** False-positive group. (a) CT findings: Contrast agent filling defect in LAA (indicated by arrow); (b) TEE findings: No abnormal condition in LA and LAA.

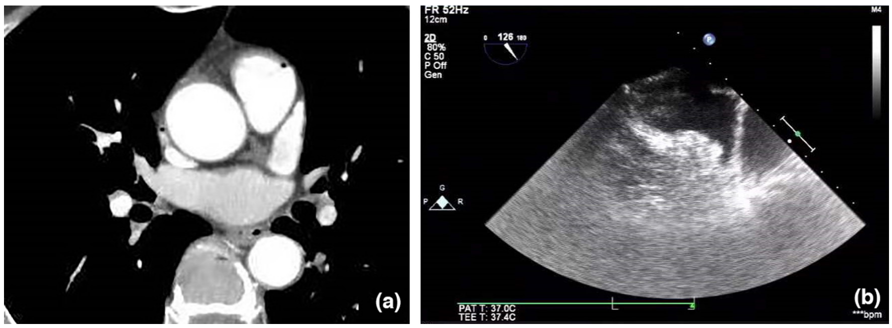


**FIGURE 4** True-negative group. (a) CT findings: No contrast agent filling defect in LAA; (b) TEE findings: No abnormal condition in LA and LAA.

Finally, 73 patients (26 females [35.6%] and 47 males [64.4%]) aged 26–86 years (average age = 63.40 ± 10.42) were enrolled in the study. Among the 73 patients, there were nine true-positive cases (12.3%), 12 false-positive cases (16.4%), and 52 true-negative cases (71.2%); the disease duration ranged from 6 months to 5 years.

## 2.2 | Examination methods

### 2.2.1 | Cardiac CTA examination

The Toshiba Aquilion One 320-row dynamic volume CT was used for scanning. The patient was instructed to take the supine position, insert his/her foot first, and raise his/her hands above the head. An electrocardiogram lead with a single end-inspiratory hold was then connected for scanning. According to the anteroposterior and lateral scout scan, the scanning range was determined as: from tracheal protuberance to cardiac diaphragmatic surface, with a range of approximately 140–160 mm, covering the entire heart.

Nonionic contrast medium (Iohexol 350) at a volume of 60–65 ml was injected via the elbow vein at a flow rate of 4.5–5.0 ml/s using a Mallinckrodt dual chamber high-pressure syringe. The flow rate and volume were adjusted according to the patient BMI and vascular condition, and 40 ml normal saline was injected at the same flow rate. Monitoring began 10 s after injection of the contrast medium, and the left ventricle was chosen as the monitoring area for manual trigger (trigger threshold—150 Hu). The interval for the second phase scan was 6 s. Scan parameters: Tube voltage—120 kV, automatic current modulation; scan slice thickness and increment—0.5 mm; rotation speed—0.35 s/circle; and mean scan time—12 ~ 15 s. After scanning, the optimal diastolic phase (75%) was selected for reconstruction (Wang et al., 2020a) and transmitted to the Advantage Workstation 4.6 workstation for the reconstruction of images based on cross-sectional images by utilizing various reconstruction methods, such as multiplanar reconstruction (MPR), maximum intensity projection (MIP), and volume rendering.

### 2.2.2 | TEE examination

All patients received ultrasound diagnosis using the Philips iE33 ultrasound system, with a 2.0–7.0MHZ ultrasound probe placed via the esophagus at a depth of 30–40 cm to the incisor. Upon examination, a 0 ~ 180° continuous scan was performed at the LAA at different angles and depths to clearly display the shape and internal structure.

### 2.3 | Postprocessing and observation of images

1. Measurement of LA anterior–posterior diameter (LAAP): As the LA is less affected by cardiac impulse, and the maximum section of the LA is usually the right inferior pulmonary vein slice, the LAAP is measured via CT mediastinum window image (window width = 350 HU, window level = 40 HU; Yang et al., 2010).
2. Measurement of LA anterior wall thickness: In the MPR image at the LA anterior area, the separation layer of the LA anterior wall and the ascending aorta (vertical to the LA anterior wall) was used to measure LA anterior wall thickness (Nakamura et al., 2011).
3. Measurement of LAA orifice diameter, area, and depth: An MPR was conducted on the axial image, parallel to the LAA long axial plane. The lateral method was used. The coronal and sagittal images were reconstructed, and the cursor was placed on three images (all at the junction of the LA and LAA); the maximum slice of the LAA orifice was adjusted on the sagittal image, and the connection line of the intersecting points of the LA and LAA tangent lines on both sides was drawn to obtain a cross-sectional image of the LAA orifice. The shape was observed, and the LAA orifice diameter and area on the tangent plane of this oblique axis were measured (Wang et al., 2010). Based on the MPR image, the longest diameter from the center of the LAA orifice to the distal side of the LAA was displayed using thin-slab MIP, and the LAA depth was measured (Wang et al., 2020b).

### 2.4 | Statistical analysis

The statistical analysis of all data was performed using the SPSS 19.0 software. Measurement data were expressed as mean ± SD, and the *t* test was conducted for two groups of data conforming to homogeneity of variance and normal distribution. The ANOVA (i.e., the *F* test) was conducted for multiple groups meeting homogeneity of variance and normal distribution (a $p$-value of $<.05$ was considered statistically significant), and the paired *q* test was further conducted for significant differences. The rank-sum test was conducted for data not conforming to homogeneity of variance and normal distribution.

The receiver operator characteristic (ROC) curve was plotted with the LAA depths in the true-positive group, false-positive group, and true-negative group to identify the cutoff points of the LAA depths available, thus helping distinguish among the true-positive group, false-positive group, and true-negative group with maximum specificity and sensitivity. A $p$-value of $<.05$ indicated that the difference was statistically significant.

## 3 | RESULTS

### 3.1 | The *F* test

(1) There were no significant differences in age, gender, and LA anterior wall thickness among the three groups ($p > .05$); (2) there were significant differences in LAD, LAA orifice long diameter, short diameter, area, and LAA depth among the three groups ($p < .05$). See Table 1 for details.

### 3.2 | The *q* test

The paired *q* test was conducted for further analysis of significant indicators (LAAP, LAA orifice long diameter, short diameter, area, and LAA depth).

1. LAAP: There was a statistical difference between the true-positive group and the true-negative group ($p < .05$) and no statistical difference when comparing the other groups ($p > .05$).
2. LAA orifice long diameter, short diameter, and area: There was a statistical difference between the true-positive group and the true-negative group ($p < .05$) as well as between the false-positive group and the true-negative group ($p < .05$), and there was no statistical difference between the true-positive group and the false-positive group ($p > .05$).
3. LAA depth: There was a statistical difference between the true-positive group and the false-positive group ($p < .05$) as well as between the true-positive group and the true-negative group

**TABLE 1** Comparison of LA- and LAA-related data between true-positive group, false-positive group, and true-negative group

| | True-positive group ($n = 9$) | False-positive group ($n = 12$) | True-negative group ($n = 52$) | $p$-Value |
|---|---|---|---|---|
| Gender (male) | 9 | 7 | 31 | .915 |
| Age | 63.33 ± 8.54 | 61.33 ± 14.83 | 63.88 ± 9.65 | .752 |
| LA anterior–posterior diameter (mm) | 50.92 ± 6.19 | 47.14 ± 8.26 | 43.25 ± 7.53 | .012 |
| LA anterior wall thickness (mm) | 2.37 ± 1.04 | 2.47 ± 0.64 | 2.78 ± 0.73 | .207 |
| LAA orifice long diameter (mm) | 33.54 ± 4.85 | 30.02 ± 3.83 | 26.14 ± 4.08 | .000 |
| LAA orifice short diameter (mm) | 25.15 ± 3.46 | 23.09 ± 3.29 | 18.83 ± 4.20 | .000 |
| LAA orifice area ($mm^2$) | 689.27 ± 163.40 | 553.82 ± 145.67 | 382.89 ± 129.29 | .000 |
| LAA depth (mm) | 56.98 ± 11.76 | 43.32 ± 9.33 | 40.92 ± 6.99 | .000 |

TABLE 2 *Q* test

| | True-positive group (*n* = 9) | False-positive group (*n* = 12) | True-negative group (*n* = 52) | *p*-Value |
|---|---|---|---|---|
| LA anterior–posterior diameter | √ | | √ | .006 |
| LAA orifice long diameter | √ | | √ | .000 |
| LAA orifice long diameter | | √ | √ | .005 |
| LAA orifice short diameter | √ | | √ | .000 |
| LAA orifice short diameter | | √ | √ | .001 |
| LAA orifice area | √ | | √ | .000 |
| LAA orifice area | | √ | √ | .000 |
| LAA depth | √ | √ | | .000 |
| LAA depth | √ | | √ | .000 |

($p<.05$), and there was no statistical difference between the false-positive group and the true-negative group ($p>.05$). See Table 2 for details.

## 3.3 | The ROC curve of LAA depth

As shown in the AUC analysis of LAA depth affecting LAA thrombus and SEC (AUC = 0.863, confidence interval = 0.718–1.000): LAA depth cutoff—50.84, the value for predicting the occurrence of LAA thrombus and SEC in patients with NVAF was the highest when the LAA depth was ≥50.84 mm, the sensitivity was 77.8%, and the specificity was 90.6%. See Figure 5 for details.

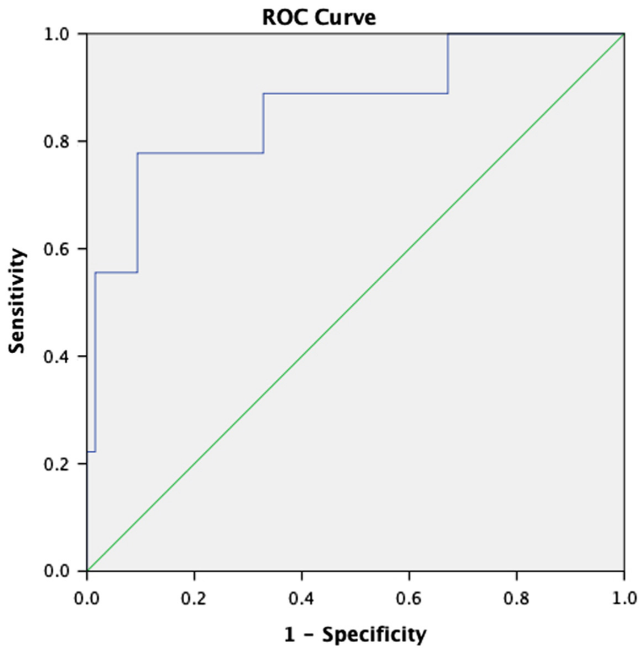


FIGURE 5 ROC curve of LAA depth.

# 4 | DISCUSSION

Cardiac CTA examination has been widely used for the evaluation of patients before ablation; however, when taking TEE as the gold standard, there exist false-positive results of LAA thrombus and SEC in the CTA evaluation, with unclear clinical significance (Ouchi et al., 2022a). Hioki et al. (2016) deemed that the filling defect of LAA on the CT result was associated with thrombus in the LAA and with the decreased blood flow rate in the LAA in patients with AF.

The volume of LA is higher in patients with AF than in others (Froehlich et al., 2019). The LAA originates in the LA and grows with the growth of LA, as they are histologically identical (Matsumoto et al., 2017). The change in the anatomic structure of the LA and LAA caused by AF (Burrell et al., 2013; Ouchi et al., 2022a; Pathak et al., 2013) is one of the reasons for the occurrence of hemodynamic disorder and thrombosis in the LAA (Lee et al., 2015). According to some studies, the size of the LA as well as the size and depth of the LAA orifice were negatively correlated with the blood flow rate in the LAA (Chen et al., 2021; Lee et al., 2014, 2015; Matsumoto et al., 2017; Miki et al., 2022; Ouchi et al., 2022b). The decreased blood flow rate in the LAA is an important factor for SEC and thrombosis, and the blood flow rate is inversely proportional to thrombosis: the lower the flow rate, the higher the thrombosis (Ma et al., 2021).

The AF anterior wall thickness, LAAP, and LAA orifice size and depth were included in the present study. Based on the TEE results, CT manifestations were classified to explore whether false-positive CT results were an objective phenomenon caused by changes in the anatomic structure of the LA and LAA. The results showed that the average value of the LAA orifice long diameter, short diameter, area, and depth in the true-negative group, false-positive group, and true-positive group increased, with statistical differences. This is consistent with the study results of Matsumoto et al. (2017), which show that an increase in the LAA orifice size and depth will further decrease the LAA blood flow rate. Lee et al. (2014) found that the risk of thromboembolism in patients with NVAF when the LAA orifice area was >3.5 $cm^2$ was higher than when the LAA orifice area was <3.5 $cm^2$. Furthermore, the average value in the three groups in the study was >3.5 $cm^2$, suggesting a risk of thrombus in the included patients.

In-group paired comparison: There was a significant difference in LAA depth between the false-positive group and the true-positive group and a significant difference in LAA orifice size between the false-positive group and the true-negative group, indicating that a false positive is an abnormal condition objectively existing between the true-positive group and the true-negative group. Compared with the results of the TEE, which failed to detect positivity at the stage, CT could detect the hemodynamic disorder in LAA earlier and more sensitively; this is consistent with the results of Ouchi et al. (2022a).

As shown in the study, the LAA structure changed continuously in the progression process of AF, leading to different CT manifestations. Due to different imaging principles, CT might be able to detect a hemodynamic disorder in the LAA earlier than TEE, and the combined application of CT+TEE could more accurately evaluate the LAA hemodynamics of patients with AF, providing references for accurate clinical decisions. There were no significant differences in gender and age among the groups, and diseases affecting the size of the heart were not included in the study; this eliminated the interference of baseline features, further demonstrating the authenticity of the study's results.

Other studies also showed that LAA parameters were not apparently associated with age or body size (Liu, 2013).

Nakamura et al. (2011) found that changes in the LA anterior wall could reflect the occurrence of AF structural remodeling, and the size of the LAAP might reflect whether the LA had increased or not. As seen in the results of the study, the averages of the LAAP and the LA anterior wall thickness in the three groups were higher than the normal value (Nakamura et al., 2011), indicating different LA changes in the cases included in the study; however, there were no significant differences in the LA anterior wall among the three groups. Therefore, it is speculated that the LA anterior wall thickness was not a risk factor for the LAA hemodynamic disorder. The LAAP showed a statistical difference between the true-negative group and the true-positive group, and the average value of the false-positive group fell in between the true-positive group and the true-negative group; thus, the false-positive group was considered to be the transitional state of the true-positive group and the true-negative group. Further studies are required.

As shown in the ROC curve plotted with LAA thrombus and the SEC defined as positive events, which was introduced in the present study for the first time, the cutoff value of the LAA depth was 50.84; the value for predicting the occurrence of LAA thrombus and SEC in patients with NVAF was the highest when the LAA depth was ≥50.84 mm, the sensitivity was 77.8%, and the specificity was 90.6%. The results indicated that the deeper the LAA, the higher the possibility of blood flow stasis, and the higher the possibility of thrombus and SEC; this is consistent with the results of Matsumoto et al. (2017).

## 5 | LIMITATIONS

This is a single-center retrospective analysis with a small sample size; hence, it cannot represent all patients with AF. Moreover, it is a retrospective study, and the AF types (paroxysmal, persistent, and permanent) could not be accurately evaluated based on medical records.

## 6 | CONCLUSION

The TEE-based CT false positive is an objectively existing state, and a CT might identify the LAA hemodynamic disorder earlier than TEE. It is concluded in the study that a CT+TEE examination for patients with AF before RFCA could accurately measure relevant data of the LA-pulmonary vein, and more accurately evaluate LAA hemodynamics of patients with AF, thus providing a better reference for clinical decisions.

### AUTHOR CONTRIBUTIONS

Tian-jiao Guo and Shu-jing Yu designed the study; Tian-jiao Guo and Ya-peng Dong searched the studies; Yan-feng Xuand Ya-peng Dong screened articles, extracted data, assessed the risk of bias and analyzed data; Tian-jiao Guowrote the manuscript.

### ACKNOWLEDGMENTS

We are particularly grateful to all the people who have given us help on our article.

### FUNDING INFORMATION

No external funding was received to conduct this study.

### CONFLICT OF INTEREST

The authors declare that they have no competing interests.

### DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

### ETHICAL APPROVAL

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the Cangzhou Central Hospital. Written informed consent was obtained from all participants.

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**How to cite this article:** Guo, T.-J., Xu, Y.-F., Dong, Y.-P., & Yu, S.-J. (2023). Study on the correlation between false-positive filling defect in LAA CT and LAA structure in patients with atrial fibrillation based on TEE. *Annals of Noninvasive Electrocardiology*, *28*, e13027. https://doi.org/10.1111/anec.13027