Association between epicardial adipose tissue and recurrence of atrial fibrillation after ablation: a propensity score-matched analysis

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Abstract
To assess the association between epicardial adipose tissue (EAT) index derived from cardiac computed tomography and atrial fibrillation (AF) recurrence after ablation by comparing with a propensity score matched non-recurrence AF patients. A total of 506 patients with AF recurrence and 174 patients without AF recurrence were enrolled in this retrospective study. Density and volume of total EAT surrounding the heart (Total-EAT) and EAT surrounding the left atrium (LA-EAT) were measured, propensity score matching (PSM) analyses were used to compare the outcomes of the two groups while controlling for confounders. Total-EAT density (HU) value (-81.27 ± 4.67 vs -84.05 ± 3.84, P < 0.001) and LA-EAT density (HU) value (-76.16 ± 4.11 vs -78.83 ± 3.81, P < 0.001) were significantly higher in the patients with AF recurrence than in those without recurrence. LA-EAT density (HU) value was significantly higher than Total-EAT (-77.50 ± 4.18 vs -82.66 ± 4.49, P = 0.000).
In a multiple logistic regression analysis, a higher LA-EAT density (odds ratio: 1.12; 95% CI: 1.02–1.22, p = 0.015) was significantly associated with the AF recurrence after adjusting for other risk factors. The LA-EAT density plays an important role in the AF recurrence after ablation. Assessment of LA-EAT density can improve ablation outcomes by refining patient selection.

Keywords Atrial fibrillation · Epicardial adipose tissue · Recurrence · Propensity score matching

Introduction
Atrial fibrillation (AF) is the most common type of supraventricular tachyarrhythmia [1]. Serious complications, such as stroke, thromboembolism, and myocardial infarction, can be induced by AF, resulting higher rates of disability and death [2–5]. Catheter-based ablation mainly targeting the pulmonary veins (PVs) has become a widely accepted operation for patients with symptomatic drug-refractory AF [6]. However, there is still a high recurrence rate after catheter ablation of AF (accounting for 10%–30%) [7].
Epicardial adipose tissue (EAT), as a special visceral adipose tissue, has been proved to be related to the occurrence, severity of AF and the recurrence of AF after catheter ablation [8, 9]. EAT has a high metabolic activity, in which the high expression of inflammatory mediators such as C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) can lead to local inflammatory reaction, which promote the occurrence of arrhythmia [10–13].
Previously, most studies showed that EAT volume (EATV) is related to recurrence after AF ablation [14], in recent years, EAT density as a newly emerging indicator has also been shown to be an independent predictor of recurrence after AF ablation [15]. However, these studies did not have effective variable control for potential risk factors for AF recurrence. Therefore, the value of the correlation between EAT density or volume and AF recurrence needs to be further explored. Statistically, propensity score matching (PSM) can match the experimental group and the control group in a certain proportion through a certain statistical method to avoid potential selection bias in observational research. In addition, in these studies, EAT measurement location includes total EAT surrounding the heart (Total-EAT) and EAT surrounding the left atrium (LA-EAT) [16, 17]. It is also reported that the concentration of inflammatory
mediators in the LA-EAT is higher than EAT surrounding other cardiac chambers [18–20]. Therefore, whether Total-EAT or LA-EAT is more suitable for studies on recurrence of AF is still inconclusive, the selection of EAT measurement location is challenging.

In this background, we aimed to investigate the correlation between EAT volume or density and AF recurrence after ablation and to compare the density of the Total-EAT and LA-EAT by applying PSM approach to adjust potential covariate imbalance.

**Materials and methods**

**Study population**

This retrospective study was approved by the Institutional Review Board. The written informed consent was waived. 782 consecutive hospitalized patients with symptomatic, drug-refractory AF referred for catheter ablation from January 1, 2017 to December 31, 2018 were enrolled in this study, all patients underwent preprocedural cardiac computed tomography angiography (CCTA) of the LA and pulmonary veins. 689 patients were included in this study according to the exclusion criteria. The clinical characteristics were retrospectively collected from the patients’ medical records. Figure 1 shows the flowchart for inclusion and exclusion.

**Ablation procedure**

Patients underwent ablation procedure the same day or the next day after the CCTA examination. The patient was placed supine in the magnetic navigation room for cryoballoon ablation of atrial fibrillation, routinely sterilized drapes, and 2% lidocaine was used for local anesthesia. Then, the right jugular vein and left femoral vein were punctured and sheathed, and electrophysiological markers were inserted through the sheath. The electrodes are measured at the coronary sinus and superior vena cava. Sinus rhythm was present in the basal state. The right femoral vein was punctured and the sheath was placed, the long sheath was placed in the superior vena cava, the atrial septal puncture was performed, the guide wire was placed in the left atrium, the cryo-balloon delivery catheter was placed, and the cryo-balloon was...
delivered through the catheter, which were placed in the left, the right, upper, and lower pulmonary veins, angiography showed good sealing and cryoaiblation, and pulmonary vein isolation was performed. Postoperative verification of pulmonary vein potential isolation is complete.

Follow-up

All patients received antiarrhythmic drugs for 8 weeks to prevent any early AF recurrence after catheter ablation. AF recurrence was defined as any evidence of an episode of atrial arrhythmia lasting more than 30 s after a 3-month blanking period [21]. All patients were followed up for at least 1 year after catheter ablation.

Propensity score matching

We used PSM approach to create a new dataset in which the probability of patients with and without AF recurrence is equal to balance patients’ baseline characteristics [22]. As shown in Table 1, before PSM, differences between the patients with and without AF recurrence in 2 variables, which were age and triglyceride. Two of the clinical variables above with a certain difference (p < 0.05) were selected to match the two groups. Propensity scores were obtained by utilizing logistic regression. Logit-transformed propensity scores matched to the nearest neighbor in a 1: 1 fashion with a caliper of 0.2 were used for the matching.

Image acquisition

All CCTA examinations were performed on a third-generation dual-source CT scanner (SOMATOM Force, Siemens Heathineers, Forchheim, Germany). CCTA was triggered 10 s after CT attenuation of region of interest (ROI) placed in the LA reached 100 HU (Hounsfield unit). A total of 50–80 mL contrast agent (Ultravist 370, Bayer Schering, Germany) was injected at the rate of 4.0–6.0 mL/s followed by a 30 mL of saline chaser. The scan mode including prospective, retrospective or high-pitch prospective modes was selected according to patients’ heart rhythm. The image parameters were as follows: tube current and tube voltage automatically determined by CARE Dose4D and CARE kV technique; detector collimation 2 × 68 × 0.6 for single energy acquisition; gantry rotation 0.25 s; pitch 0.15–0.25; 512 × 512 pixel matrix size. Images were reconstructed at the kernel of Bv40, with the image thickness of 0.75 mm and increment of 0.4 mm. The phase with best image quality was picked for imaging measurements and analysis. All images were analyzed on the commercial

Table 1  Baseline Characteristics of population

| Characteristic       | Before matching (680 patients) | After matching (348 patients) |
|----------------------|--------------------------------|-------------------------------|
|                      | Non-recurrence (506 patients) | Recurrence (174 patients)     | Non-recurrence (174 patients) | Recurrence (174 patients) |
| Age                  | 62.00 (55.00, 67.00)           | 64.00 (57.00, 69.25)          | 63.00 (58.00, 69.00)          | 64.00 (57.00, 69.25)      |
|                      | 0.007                          | 0.901                         | 0.780                         | 0.902                      |
| BMI (kg/m²)          | 24.56 (22.65, 26.93)           | 24.68 (22.90, 26.75)          | 24.49 (22.49, 27.23)          | 24.68 (22.90, 26.75)      |
|                      | 0.901                          | 0.281                         | 0.739                         | 0.793                      |
| TC (mmol/L)          | 4.31 ± 0.98                    | 4.21 ± 1.01                   | 4.18 ± 1.00                   | 4.22 ± 1.01                |
|                      | 0.244                          | 0.902                         | 0.843                         | 0.739                      |
| LDL-C (mmol/L)       | 2.65 (1.97, 3.14)              | 2.53 (1.87, 3.09)             | 2.53 ± 0.81                   | 2.54 ± 0.87                |
|                      | 0.244                          | 0.241                         | 0.843                         | 0.739                      |
| HDL-C (mmol/L)       | 1.16 (1.01, 1.35)              | 1.18 (1.02, 1.36)             | 1.16 (1.02, 1.39)             | 1.18 (1.02, 1.36)          |
|                      | 0.600                          | 0.604                         | 0.604                         | 0.604                      |
| TG (mmol/L)          | 1.42 (1.03, 1.91)              | 1.27 (0.90, 1.72)             | 1.26 (0.89, 1.72)             | 1.27 (0.90, 1.72)          |
|                      | 0.019                          | 0.992                         | 0.997                         | 0.992                      |
| Heart rate           | 78.53 ± 10.96                  | 79.50 ± 12.86                 | 77.45 ± 15.11                 | 78.26 ± 13.20              |
|                      | 0.336                          | 0.592                         | 0.592                         | 0.592                      |
| Gender               | Male                           | 323 (63.8%)                   | 323 (63.8%)                   | 323 (63.8%)                |
|                      | 0.992                          | 0.911                         | 0.911                         | 0.911                      |
|                      | Female                         | 183 (36.2%)                   | 183 (36.2%)                   | 183 (36.2%)                |
| Diabetes             | Absent                         | 434 (85.8%)                   | 434 (85.8%)                   | 434 (85.8%)                |
|                      | 0.550                          | 0.654                         | 0.654                         | 0.654                      |
|                      | Presence                        | 72 (14.2%)                    | 72 (14.2%)                    | 72 (14.2%)                 |
| Hyperlipidemia       | Absent                         | 333 (65.8%)                   | 333 (65.8%)                   | 333 (65.8%)                |
|                      | 0.446                          | 0.726                         | 0.726                         | 0.726                      |
|                      | Presence                        | 173 (34.2%)                   | 173 (34.2%)                   | 173 (34.2%)                |
| Hypertension         | Absent                         | 254 (50.2%)                   | 254 (50.2%)                   | 254 (50.2%)                |
|                      | 0.337                          | 0.284                         | 0.284                         | 0.284                      |
|                      | Presence                        | 252 (49.8%)                   | 252 (49.8%)                   | 252 (49.8%)                |
| Smoking              | Absent                         | 354 (70.0%)                   | 354 (70.0%)                   | 354 (70.0%)                |
|                      | 0.367                          | 0.381                         | 0.381                         | 0.381                      |
|                      | Presence                        | 152 (30.0%)                   | 152 (30.0%)                   | 152 (30.0%)                |
| Statin               | Absent                         | 381 (75.3%)                   | 381 (75.3%)                   | 381 (75.3%)                |
|                      | 0.445                          | 0.792                         | 0.792                         | 0.792                      |
|                      | Presence                        | 125 (24.7%)                   | 125 (24.7%)                   | 125 (24.7%)                |

p value < 0.05 was considered as statistically significant. BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.
postprocessing workstation (SyngoVia, VB20, Siemens Healthineers, Forchheim, Germany).

**EAT morphological measurement**

EAT were semi-automatically segmented by a dedicated software (Cardiac Risk Analysis, Research Frontier, SyngoVia, Siemens Healthineers). The EAT mask was then loaded into the Radiomics software (Research Frontier, SyngoVia, Siemens Healthineers) to delineate LA-EAT and quantify EAT and LA-EAT [23]. Axial images were used to delineate the LA-EAT mask from the pulmonary artery to the coronary sinus, then we trimmed along the LA, pulmonary veins, and left atrial appendages using axial, coronal, and sagittal slices. The contour delineation was checked and manually trimmed with EAT as a reference if necessary. Adipose tissue was defined as voxels between −190 and −30 Hu. Meanwhile, the volumes and densities of EAT and LA-EAT were measured. (Fig. 2) An experienced radiologist, who was blinded to patients’ clinical characteristics, performed the measurement independently and remeasured after one month to avoid imaging recognition.

**Statistical analysis**

The statistical analysis was performed on SPSS version 25.0 (Statistical Product and Service Solutions, IBM; Armonk, NY, USA). Normality was examined with the Kolmogorov–Smirnov test. The means ± standard deviations for normally distributed variables and medians (25th–75th percentiles) for non-normally distributed variables were calculated. Categorical variables were compared by using the χ² test. The Student’s t-test and the Wilcoxon rank-sum test were used for comparing continuous variables. Univariate and multivariate analyses of independent risk factors for recurrence of AF were performed using logistic regression analysis. The lesion segmentation was performed in the analysis step integrated on the Radiomics prototype (Frontier, VB10, Siemens). The intraclass correlation coefficient (ICC) was reported for intra-observer reliability. All probability values reported were 2-sided, and a probability value < 0.05 was considered statistically significant.

**Results**

**Baseline Characteristics of population**

A total of 9 patients (1.3%) were lost during follow-up and excluded from the results. 174 patients developed AF recurrence while 506 patients remained free of AF recurrence after ablation within 1 year. The baseline characteristics of each group are presented in Table 1. Between group analysis revealed that 11 factors were equal in the two original groups (p > 0.05). Differences in age and triglyceride were statistically significant (p < 0.05). After PSM, variables of baseline characteristics were shown no significant differences in the matched non-recurrence group (n = 174) and recurrence group (n = 174). Consequently, the difference of other risk factors which might have impact on EAT and AF have been eliminated, permitting fully examine the association between EAT and AF recurrence. In the following sections, all statistical comparisons were based on the matched population.

![Fig. 2 A, B Axis view of the epicardial adipose tissue. A EAT volume. B LA-EAT volume. EAT epicardial adipose tissue, LA-EAT epicardial adipose tissue around the left atrium](image-url)
Comparison of EAT between patients with and without AF recurrence After matching

The intra-observer variability ICC of the LA-EATV and LA-EAT densities are 0.997 and 0.988, respectively, showing an excellent agreement.

The volume of LA (mL) (133.65 ± 38.70 vs 116.62 ± 40.30, P < 0.001) was significantly higher in the patients with AF recurrence than in those without recurrence. No difference of the volume of Total-EAT (mL) (126.53 ± 47.03 vs 129.19 ± 48.59, P = 0.604) and LA-EAT (mL) (25.00 ± 12.45 vs 23.63 ± 12.30, P = 0.302) was found. Total-EAT density (HU) value (−81.27 ± 4.67 vs −84.05 ± 3.84, P < 0.001) and LA-EAT density (HU) value (−76.16 ± 4.11 vs −78.83 ± 3.81, P < 0.001) were significantly higher in the patients with AF recurrence than in those without recurrence. (Table 2).

The overall comparison between Total-EAT and LA-EAT density in the whole cohort: LA-EAT density (HU) value was significantly higher than Total-EAT (−77.50 ± 4.18 vs −82.66 ± 4.49, P = 0.000).

Logistic regression analysis

The LA volume, Total-EAT density, and LA-EAT density were selected by univariate analysis (Table 3). AF risk factors and our measurement parameters were included in the multiple logistic regression analysis, including age, sex, BMI, diabetes, hypertension, hyperlipidemia, TC, TG, HDL-C, LDL-C, smoking, statin, LA volume, EAT density and LA-EAT density. The density of LA-EAT (odds ratio: 1.12; 95% CI 1.02–1.22, p = 0.015) was significantly associated with the AF recurrence, as well as the LA volume (odds ratio: 1.01; 95% CI 1.01–1.02, p < 0.001) after adjusting for baseline characteristics (Table 3). The cut-off value of LA-EAT density was −78.45 HU for predicting AF recurrence.

Discussion

The present study has found that LAV, Total-EAT density and LA-EAT density of recurrent group was significantly higher than the matched groups. In addition, LAV and LA-EAT density were independent predictors of AF recurrence. Furthermore, the density of LA-EAT was significantly higher than that of Total-EAT.

The density of inflamed tissues has a higher CT value than that of non-inflamed tissues [24]. We found that LA-EAT density was associated with post-ablation recurrence of AF. Each increase in the average CT value of LA-EAT by 1 unit increases the risk of AF recurrence by 1.12 times. As a part of the visceral adipose tissue in the human body, EAT is located in the pericardial sac and is closely connected to the outer wall of the myocardium [14]. At present, the specific pathogenesis of EAT affecting AF is still unclear, previous studies thought that the occurrence and development of AF may be a process involving multiple factors, including abnormal electrophysiological conduction, EAT...
secretion of adipokines, EAT activates autonomic nerves, EAT releases inflammatory mediators, etc. [25, 26]. Local inflammatory processes play a role in the pathophysiology of AF. Inflammation markers, such as CRP, IL-6 and TNF-α are related to the occurrence, severity and recurrence of AF after ablation [27–30]. These markers are secreted by EAT, which may have a local pro-inflammatory effect on the adjacent atrial myocardium, thereby promoting the occurrence and development of arrhythmia.

In addition, we also found that the density of LA-EAT was significantly higher than that of Total-EAT. Indeed, some studies have pointed out that LA-EAT may be a better independent risk factor associated with AF severity or prognosis than total EAT [31, 32]. Atrial biopsies from patients with AF have shown the infiltration of inflammatory cells [33]. Therefore, the study of the correlation between EAT and recurrence of AF should pay more attention to the role of LA-EAT in it. On the other hand, there is heterogenicity of EAT according to the anatomical location. EAT is concentrated in the atroioventricular (AV) and interventricular (IV) grooves, along the major branches of the coronary arteries, around the atria, over the free wall of the right ventricle (RV) and over the apex of the left ventricle (LV). Gaborit B et al. found the different transcriptomic signatures of the three components (i.e., peri-coronary, peri-atrial, and periventricular sites) of EAT [20]. Similarly, as a part of EAT, peri-coronary adipose tissue was found with different attenuation among vessels branches and locations [34, 35]. The difference between total-EAT and LA-EAT density in our study also partially proved the heterogenicity of total EAT.

Previous studies showed that the volume of the Total-EAT and LA-EAT are associated with AF recurrence after catheter ablation [36, 37]. In our study, the Total-EAT and LA-EAT volumes of patients with recurrence after AF ablation were higher than those of patients without recurrence, but the difference was not statistically significant. Since we balance the confounding factors with PSM, this may indicate that the density of the EAT may more accurately reflect the relationship between EAT and the prognosis of AF.

We also found that the patients with AF recurrence had a larger LA, suggestive of progressive atrial remodeling. Left atrial volume enlargement is risk predictor after ablation of AF because AF causes remodeling and fibrosis of the LA [38]. Cardiac endothelin-1 expression correlates with enlarged left atrium size and responds to the wall stress caused by enlarged left atrium, thus promoting hypertrophy of myocytes and fibrosis of myocardial interstitium. Atrial fibrosis in patches can cause slow conduction and change dynamic repolarization in some areas, consequently shifting the initiation focus and AF maintenance to the left atrium from the pulmonary veins [39, 40]. In this case, radiofrequency ablation may be insufficient, resulting in an increased rate of recurrence.

This study still has certain limitations: (1) This study is a single-center retrospective study with a small sample size. Further study should consider expanding the sample for further confirmation. (2) PSM can only control known risk factors, and there may be some unknown factors that bias the results, but we have tried our best to control all the indicators that can be collected. (3) Statistics about the time of recurrence should be as accurate as possible in follow-up studies. (4) Inflammatory biomarkers were not included in this retrospective study. Further prospective studies incorporating inflammatory biomarker need to be performed. (5) The enhanced images were used for analysis in this study, which might potentially increase the CT value of the EAT. But unified scanning and injection protocol was performed in our patients, which may avoid the impact of enhancement on the comparison of density between recurrence and non-recurrence cohorts.

### Conclusion

LA-EAT density and LAV were independent predictors of AF recurrence. In addition, the density of LA-EAT was significantly higher than that of Total-EAT. LA-EAT mediated inflammation plays an important role in the prognosis of AF. Therefore, assessment of LA-EAT density can improve ablation outcomes by refining patient selection.

### Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MY, WB, ZX, LQ and NZh. Conceptualization, resources, and methodology were performed by WY, and FY. The first draft of the manuscript was written by MY. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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### Declarations

#### Conflict of interest

The authors declare that they have no conflict of interest.

#### Ethical approval

The approval for this study had been granted by the local Institutional Reviewboard prior to its conduct and informed consent was waived. The study therefore had been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its lateramendments. No patient identifiers were collected.
and details that might disclose the identity of the subjects under study should be omitted.

References

1. Björck S, Palaszewski B, Friberg L, Bergfeldt L (2013) Atrial fibrillation, stroke risk, and warfarin therapy revisited: a population-based study. Stroke 44:3103–3108. https://doi.org/10.1161/ strokeaha.113.002329

2. Pastori D, Pignatelli P, Angelico F, Farcomeni A, Del Ben M, Vicario T et al (2015) Incidence of myocardial infarction and vascular death in elderly patients with atrial fibrillation taking anticoagulants: relation to atherosclerotic risk factors. Chest 147:1644–1650. https://doi.org/10.1378/chest.14-2414

3. Gómez-Outes A, Lagunar-Ruíz J, Terleira-Fernández AI, Calvo-Cabrillón E (2016) Causes of Death in Anticoagulated Patients With Atrial Fibrillation. J Am Coll Cardiol 68:2508–2521. https://doi.org/10.1016/j.jacc.2016.09.944

4. Pokorney SD, Piccini JP, Stevens SR, Patel MR, Pieper KS, Halperin JL et al (2016) Cause of death and predictors of all-cause mortality in anticoagulated patients with nonvalvular atrial fibrillation: data from ROCKET AF. J Am Heart Assoc 5:e002197. https://doi.org/10.1161/jaha.115.002197

5. Lee HY, Yang PS, Kim TH, Uhm JS, Pak HN, Lee MH et al (2017) Atrial fibrillation and the risk of myocardial infarction: a nation-wide propensity-matched study. Sci Rep 7:12716. https://doi.org/10.1038/s41598-017-13061-4

6. Takahashi A (2010) Catheter ablation is established as a treatment option for atrial fibrillation—is catheter ablation established as a treatment option of atrial fibrillation? (Pro). Circ J 74:1972–1977. https://doi.org/10.1253/circj.74-00693

7. Yi F, Hou W, Zhou C, Yin Y, Lu S, Duan C et al (2019) Radiofrequency ablation versus antiarrhythmic drug therapy for atrial fibrillation: meta-analysis of safety and efficacy. J Cardiovasc Pharmacol 73:241–247. https://doi.org/10.1097/jcpc.0000000000000654

8. Al Chekakie MO, Welles CC, Metoyer R, Ibrahim A, Shapira AR, Cytron J et al (2010) Pericardial fat is independently associated with human atrial fibrillation. J Am Coll Cardiol 56:784–788. https://doi.org/10.1016/j.jacc.2010.03.071

9. Tsao HM, Wu WC, Wu MH, Tai CT, Lin YJ, Chang SL et al (2011) Quantitative analysis of quantity and distribution of epicardial adipose tissue surrounding the left atrium in patients with atrial fibrillation and effect of recurrence after ablation. Am J Cardiol 107:1498–1503. https://doi.org/10.1016/j.amjcard.2011.01.027

10. Acet H, Ertas F, Akil MA, Oylumu M, Polat N, Yildiz A et al (2014) New inflammatory predictors for non-valvular atrial fibrillation: echocardiographic epicardial fat thickness and neutrophil to lymphocyte ratio. Int J Cardiovasc Imaging 30:81–89. https://doi.org/10.1007/s10554-013-0317-4

11. Mazurek T, Kiliszek M, Kobylecka M, Skubiś-Gluchowska J, Kochman J, Filipiak K et al (2014) Relation of proinflammatory activity of epicardial adipose tissue to the occurrence of atrial fibrillation. Am J Cardiol 113:1505–1508. https://doi.org/10.1016/j.amjcard.2014.02.005

12. Packer M (2019) Drugs that ameliorate epicardial adipose tissue inflammation may have discordant effects in heart failure with a preserved ejection fraction as compared with a reduced ejection fraction. J Card Fail 25:986–1003. https://doi.org/10.1016/j.cardfail.2019.09.002

13. Liu Q, Zhang F, Yang M, Zhong J (2020) Increasing level of interleukin-1β in epicardial adipose tissue is associated with persistent atrial fibrillation. J Interferon Cytokine Res 40:64–69. https://doi.org/10.1089/jir.2019.0098

14. Wong CX, Ganesan AN, Selvanayagam JB (2017) Epicardial fat and atrial fibrillation: current evidence, potential mechanisms, clinical implications, and future directions. Eur Heart J 38:1294–1302. https://doi.org/10.1093/euheartj/ehw045

15. Ciuffo L, Nguyen H, Marques MD, Aronis KN, Sivasambu B, de Vasconcelos HD et al (2019) Periatrial Fat Quality Predicts Atrial Fibrillation Ablation Outcome. Circ Cardiovasc Imaging 12:e008764. https://doi.org/10.1161/circimaging.118.008764

16. Batal O, Schoenhagen P, Shao M, Ayyad AE, Van Wagener DR, Halliburton SS et al (2010) Left atrial epicardial adiposity and atrial fibrillation. Circ Arrhythm Electrophysiol 3:230–236. https://doi.org/10.1161/circcep.110.957241

17. Kogo H, Sezai A, Osaka S, Shiono M, Tanaka M (2019) Does epicardial adipose tissue influence postoperative atrial fibrillation? Ann Thorac Cardiovasc Surg 25:149–157. https://doi.org/10.5761/atcs.oa.18-00212

18. Nguyen BL, Fishbein MC, Chen LS, Chen PS, Masoor S (2009) Histopathological substrate for chronic atrial fibrillation in humans. Heart Rhythm 6:454–460. https://doi.org/10.1016/j.hrthm.2009.01.010

19. Marcus GM, Smith LM, Ordovas K, Scheinman MM, Kim AM, Badhwar N et al (2010) Intracardiac and extracardiac markers of inflammation during atrial fibrillation. Heart Rhythm 7:149–154. https://doi.org/10.1016/j.hrthm.2009.10.004

20. Gaborit B, Venteclef N, Ancel P, Pelloux V, Gariboldi V, Leprince P et al (2015) Human epicardial adipose tissue has a specific transcriptional signature depending on its anatomical per-atrial, peri-ventricular, or peri-coronary location. Cardiovasc Res 108:62–73. https://doi.org/10.1093/cvr/cvw208

21. Calkins H, Hindricks G, Cappato R, Kim YH, Saab EB, Aguina L et al (2017) 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Heart Rhythm 14:e275–e444. https://doi.org/10.1016/j.hrthm.2017.05.012

22. Austin PC (2011) An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivariate Behav Res 46:399–424. https://doi.org/10.1080/00273171.2011.568754

23. Wells MG, Lades F, Muehlberg A, Suebaing M (2019) General purpose radiomics for multi-modal clinical research. InMedical Imaging 2019: Computer-Aided Diagnosis 2019 Mar 13. Vol 10950, pp 1047–1054. SPIE

24. Zhang M, Kono M (1997) Solitary pulmonary nodules: evaluation of blood flow patterns with dynamic CT. Radiology 205:471–478. https://doi.org/10.1148/radiology.205.2.9356631

25. Venteclef N, Guglielmi V, Balse E, Gaborit B, Cotillard A, Atassi F et al (2015) Human epicardial adipose tissue induces fibrosis of the atrial myocardium through the secretion of adipo-fibrokines. Eur Heart J 36:795–805a. https://doi.org/10.1093/eurheartj/ehv099

26. Vyas V, Lambiase P (2019) Obesity and Atrial Fibrillation: Epidemiology, Pathophysiology and Novel Therapeutic Opportunities. Arrhythm Electrophysiol Rev 8:28–36. https://doi.org/10.15420/ater.2018.76.2

27. Chung MK, Martin DO, Sprecher D, Wazni O, Kanderian A, Cardes CA et al (2001) C-reactive protein elevation in patients with atrial arrhythmias: inflammatory mechanisms and persistence of atrial fibrillation. Circulation 104:2886–2891. https://doi.org/10.1161/hc4091.101760

28. Aviles RJ, Martin DO, Apperson-Hansen C, Houghtaling PL, Rautaharju P, Kronmal RA et al (2003) Inflammation as a risk factor...
factor for atrial fibrillation. Circulation 108:3006–3010. [https://doi.org/10.1161/01.CIR.0000103131.70301.4f]

29. Malouf JF, Kanagala R, Al Atawi FO, Rosales AG, Davison DE, Murali NS et al (2005) High sensitivity C-reactive protein: a novel predictor for recurrence of atrial fibrillation after successful cardioversion. J Am Coll Cardiol 46:1284–1287. [https://doi.org/10.1016/j.jacc.2005.06.053]

30. Rotter M, Jaïs P, Vergnes MC, Nurden P, Takahashi Y, Sanders P et al (2006) Decline in C-reactive protein after successful ablation of long-lasting persistent atrial fibrillation. J Am Coll Cardiol 47:1231–1233. [https://doi.org/10.1016/j.jacc.2005.12.038]

31. Liu T, Li G. Periatrial epicardial fat, local pro- and anti-inflammatory balance, and atrial fibrillation. J Am Coll Cardiol 2011;57:1249. [https://doi.org/10.1016/j.jacc.2010.09.068]

32. Shin SY, Yong HS, Lim HE, Na JO, Choi CU, Choi JI et al (2011) Total and interatrial epicardial adipose tissues are independently associated with left atrial remodeling in patients with atrial fibrillation. J Cardiovasc Electrophysiol 22:647–655. [https://doi.org/10.1111/j.1540-8167.2010.01993.x]

33. Frustaci A, Chimenti C, Bellocci F, Morgante E, Russo MA, Maseri A (1997) Histological substrate of atrial biopsies in patients with lone atrial fibrillation. Circulation 96:1180–1184. [https://doi.org/10.1161/01.cir.96.4.1180]

34. Hell MM, Achenbach S, Schuhbaeck A, Klinghammer L, May MS, Marwan M (2016) CT-based analysis of pericoronary adipose tissue density: Relation to cardiovascular risk factors and epicardial adipose tissue volume. J Cardiovasc Comput Tomogr 10:52–60. [https://doi.org/10.1016/j.jcct.2015.07.011]

35. Balcer B, Dykun I, Schlosser T, Forsting M, Rassaf T, Mahabadi AA (2018) Pericoronary fat volume but not attenuation differentiates culprit lesions in patients with myocardial infarction. Atherosclerosis 276:182–188. [https://doi.org/10.1016/j.atherosclerosis.2018.05.035]

36. Sephere Shamloo A, Dagres N, Dinov B, Sommer P, Husser-Bollmann D, Bollmann A et al (2019) Is epicardial fat tissue associated with atrial fibrillation recurrence after ablation? A systematic review and meta-analysis. Int J Cardiol Heart Vasc 22:132–138. [https://doi.org/10.1016/j.ijchx.v.2019.01.003]

37. Nagashima K, Okumura Y, Watanabe I, Nakai T, Ohkubo K, Kofune T et al (2011) Association between epicardial adipose tissue volumes on 3-dimensional reconstructed CT images and recurrence of atrial fibrillation after catheter ablation. Circ J 75:2559–2565. [https://doi.org/10.1253/circj.cj-11-0554]

38. D’Ascenzo F, Corleto A, Biondi-Zoccai G, Anselmino M, Ferraris F, di Biase L et al (2013) Which are the most reliable predictors of recurrence of atrial fibrillation after transcatheter ablation?: A meta-analysis. Int J Cardiol 167:1984–1989. [https://doi.org/10.1016/j.ijcard.2012.05.008]

39. Krummen DE, Swarup V, Narayan SM (2015) The role of rotors in atrial fibrillation. J Thorac Dis 7:142–151. [https://doi.org/10.3978/j.issn.2072-1439.2014.11.15]

40. Mayyas F, Niebauer M, Zurick A, Barnard J, Gillinov AM, Chung MK et al (2010) Association of left atrial endothelin-1 with atrial rhythm, size, and fibrosis in patients with structural heart disease. Circ Arrhythm Electrophysiol 3:369–379. [https://doi.org/10.1161/circep.109.924985]

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