Left Atrial Epicardial Adiposity and Atrial Fibrillation

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Abstract

**Background:** Atrial fibrillation (AF) has been linked to inflammatory factors and obesity. Epicardial fat is a source of several inflammatory mediators related to the development of CAD. We hypothesized that peri-atrial fat may have a similar role in the development of AF.

**Methods and Results:** Left atrium (LA) epicardial fat pad thickness was measured in consecutive cardiac CT angiograms performed for CAD or AF. Patients were grouped by AF burden: No (N=73), Paroxysmal (60), or Persistent (36) AF. In a short axis view at the mid LA, peri-atrial epicardial fat thickness was measured at the esophagus (LA-ESO), main pulmonary artery and thoracic aorta; retrosternal fat was measured in axial view (right coronary ostium level). LA-area was determined in the 4-chamber view. LA-ESO fat was thicker in patients with persistent AF versus paroxysmal AF (p=0.011) or no AF (p=0.003). LA-area was larger in patients with persistent AF than paroxysmal AF (p=0.004) or without AF (p<0.001). LA-ESO was a significant predictor of AF burden even after adjusting for age, BMI and LA area (odds ratio 5.30, 95%CI 1.39-20.24, p=0.015). A propensity score-adjusted multivariable logistic regression that included age, BMI, LA area and comorbidities was also performed and the relationship remained statistically significant (p=0.008).

**Conclusions:** Increased posterior LA fat thickness appears to be associated with AF burden independent of age, BMI, or LA-area. Further studies are necessary to examine cause and effect, and if inflammatory, paracrine mediators explain this association.

**Key words:** Atrial fibrillation, inflammation, obesity, pericardium, tomography
**Abbreviations:**

AF: atrial fibrillation

BMI: Body Mass Index

CABG: Coronary Artery Bypass Grafting

CAD: Coronary Artery Disease

CHF: Congestive Heart Failure

CKD: Chronic kidney disease

CRP: C-reactive protein

CT: Computed tomography

DM: Diabetes mellitus

ESO: Esophagus

HPL: Hyperlipidemia

HTN: Hypertension

LA: Left atrium

PA: Main pulmonary artery

PVI: Pulmonary vein isolation

RS: Retrosternal

TA: Thoracic aorta
Background:

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice (1) and is associated with increased morbidity and mortality (2). While AF pathophysiology is complex, increasing evidence supports mechanistic links between inflammation and AF. AF has been associated with inflammatory conditions that involve the heart such as pericarditis and myocarditis (3, 4). The incidence of AF after coronary artery bypass grafting (CABG) is increased, with a peak frequency coincident with peak postoperative C-reactive protein (CRP) levels (5). In addition, CRP appears to be higher in patients with non-postoperative AF and is associated with AF duration and persistence (6-8). Higher levels of CRP predict the future development of AF in patients without prior history of AF (9). Furthermore, atrial biopsies from patients with AF have shown evidence of inflammatory cells, suggesting that inflammation plays a role in the pathogenesis of AF (10-11).

A relationship has been described between obesity, epi/pericardial fat, inflammation, and coronary atherosclerosis. Perivascular adipocytes secrete inflammatory cytokines, and the extent of epicardial fat is associated with the severity of coronary artery disease (CAD) (12-16). Obesity is a risk factor for AF (17) and has been associated with pericardial fat (13), but the potential relationship of peri-atrial epicardial fat and AF has not been previously described. We sought to test the hypothesis that peri-atrial epicardial fat is associated with AF.

Methods:

Patient Population
We analyzed data from 169 consecutive patients, who underwent consecutive cardiac computed tomography (CT) angiograms between January and May 2008, for evaluation of AF or CAD. Subjects were identified from a cardiovascular CT registry. CT studies obtained for AF were performed in evaluation for AF catheter ablation (pulmonary vein isolation, [PVI]). Typically candidates for PVI at our institution are patients who have symptomatic AF despite medical therapy. The study was approved by the Institutional Review Board with waiver of consent for medical records review and performed according to institutional guidelines.

Data retrospectively collected from patient medical records included age, sex, body mass index (BMI) (Kg/m²), comorbidities (hypertension [HTN], hyperlipidemia [HPL], diabetes mellitus [DM], chronic kidney disease [CKD], CAD, congestive heart failure [CHF], and thyroid disease), history of AF, AF burden, treatment by PVI. CAD, CHF and AF burden were defined as per published guidelines (18-20). Patients were categorized according to their highest AF burden (no history of AF, paroxysmal AF, and persistent AF). Paroxysmal AF was defined as recurring AF terminating in 7 days or less. Persistent AF indicated a history of AF sustaining beyond 7 days.

**Imaging Protocol**

Patients with known AF (N=95) were evaluated with cardiac CT angiography for PVI. Multi-detector row CT technology was employed (Definition, Siemens Medical Solutions, Erlangen, Germany or Brilliance 64, Philips Medical Systems, Cleveland, Ohio). The specific imaging protocol for the clinically indicated scans was adapted to minimize radiation exposure for each patient while insuring acceptable image quality. Electrocardiogram-referenced scans were performed following intravenous administration of contrast material. Because pulmonary vein assessment was the primary clinical goal, 1.5 mm thick images were reconstructed. Patients
evaluated for CAD (N=74) were imaged using the same scanner models. Again, the specific imaging protocol was adapted for each patient and the electrocardiogram-referenced scan performed following the intravenous administration of contrast material. For evaluation of the coronary arteries, 0.75 mm thick slices were reconstructed. For optimal visualization of coronary anatomy, patients were pre-medicated with sublingual nitroglycerin and intravenous beta-adrenergic blocker for coronary dilatation and heart rate control, respectively.

**Image Analysis:**

Using a standard clinical workstation (Leonardo, Siemens), advanced 3-dimensional off-line post-processing was performed. The 3-dimensional CT dataset was reconstructed to obtain standard cardiac views as used in echocardiography. We first reconstructed standard 2- and 4-chamber views. LA size was determined by manually tracing the LA borders in the 4-chamber view (making sure to exclude the pulmonary veins) and using computer software that calculates the outlined area. The short axis view was reconstructed as a plane perpendicular to the long axis of these two views at the level of the mid LA (Figure 1). In this short axis view, the peri-atrial epicardial fat thickness was measured (in cm) as the shortest distance between the mid left atrium (LA) wall and three anatomical landmarks: esophagus (LA-ESO), main pulmonary artery (LA-PA), and descending thoracic aorta (LA-TA) [Figures 2 and 3]. These measurements were prospectively determined, based on preliminary reviews of representative CT scans before starting the study, which showed the esophagus, pulmonary artery and thoracic aorta were readily identifiable anatomic structures which could be used to measure LA epicardial fat. Retrosternal fat thickness (RS) was measured at the level of the right coronary artery (RCA) ostium (Figure 4) in the axial view. RS fat was measured based on similar measurements of epicardial fat thickness used in previous echocardiographic studies evaluating the association of
epicardial fat and CAD (14). Measurements were made utilizing digital calipers by a single investigator (O.B.) with an intra-observer reproducibility of 0.957 (95% CI 0.909-0.979, intra-class correlation, same below) on measurements of epicardial fat and 0.984 (95% CI 0.937-0.996) on measurements of LA-area. In a sample of 30 randomly selected patients, the inter-observer reliability was 0.948 (95% CI 0.912-0.969) on measurements of epicardial fat and 0.978 (95% CI 0.954-0.990) on measurements of LA-area (by O.B. and P.S.). AF status was blinded to the investigators at the time of epicardial fat measurements.

**Statistical Methods:**

AF burden was analyzed by grade (no AF=0, paroxysmal=1, persistent=2). Continuous variables were compared using one-way analysis of variance and were reported as mean ± standard deviation if normally distributed, or they were compared using Kruskal-Wallis test and were reported as median ± interquartile range if not normally distributed. Pearson chi-square analysis was used to compare categorical variables. Bonferroni adjustment for multiple comparisons was applied following the overall 3 group comparisons.

Univariable and multivariable ordinal logistic regression models were constructed to test the association between peri-atrial LA-ESO fat thickness and AF burden. In the multivariable model the covariates were age, BMI and LA area. The proportional odds assumption was tested. Propensity scores were estimated by running logistic regression using the 75 percentile of LA-ESO as the response variable and age, BMI, LA area, and patient characteristics (gender, hypertension, hyperlipidemia, diabetes mellitus, CAD, congestive heart failure, and hypothyroidism) as the covariates. A propensity score-adjusted multivariable logistic regression was then performed to adjust for imbalances of the registry data.
Missing data of LA-ESO and BMI were imputed using overall mean imputation, and the imputed data were used to run logistic regressions as a supplement to the analyses of the original data. Statistical testing was 2-sided and results were considered statistically significant at the level of p<0.05, or at p<0.015 after the Bonferroni correction. All analyses were conducted using SAS 9.1.3 (SAS Institute, Cary, NC).

Results:

Patient characteristics

Patient characteristics of the entire study are summarized in Table 1. The mean age of the 169 patients included in this study was 54.6 ± 13.2 years (range 15-82 years); 34.9% of patients were female. The mean body mass index (BMI) was 29.2 ± 6.1 Kg/m². In this study population, 73 (43.2%) patients did not have AF, 60 (35.5%) had paroxysmal AF, and 36(21.3%) had persistent AF. Comorbid conditions included CAD (15.4%), HTN (42.9%), HPL (41.6%), DM (7.1%), CHF (5.8%), CKD (1.9%) and thyroid disease (12.3%).

Characteristics by AF burden

As shown in Table 1, patients without AF were younger than patients with paroxysmal AF (p=0.001) and persistent AF (p=0.007), respectively. The BMI of patients without AF (p=0.311) or with paroxysmal AF (p=0.018) and patients with persistent AF was not significantly different at the 0.015 significance level. The trend of a greater prevalence of CAD in patients without AF (vs. paroxysmal AF p=0.019; vs. persistent AF p=0.003) likely reflected the initial indications for CT angiography. Patients specifically evaluated for CAD had a higher pretest probability of having CAD than patients who had the cardiac CT prior to PVI. Differences in other comorbid factors were not statistically significant.
**Peri-atrial and retrosternal fat and LA-area versus AF burden**

Peri-atrial and retrosternal fat measurements by AF burden are summarized in Table 2. Patients with persistent AF had a significantly thicker LA-ESO fat pad as compared to patients with no AF (p=0.003) or with paroxysmal AF (p=0.011). A stepwise trend toward increasing LA-ESO thickness was observed in patients with increasing AF burden and is depicted in figure 5.

The thickness of the retrosternal fat pad (RS) at the level of the RCA takeoff was compared according to AF burden (table 2). RS fat pad thickness was not associated with AF burden.

LA-Area was found to be larger in patients with persistent AF than in paroxysmal AF (p=0.004) or in patients without AF (p<0.001). This is shown in table 2.

**Regression analysis:**

The association between AF burden by grade (no AF=0, paroxysmal=1, persistent=2) and peri-atrial LA-ESO fat thickness was assessed by ordinal logistic regression. Univariately, LA-ESO was a significant predictor of AF burden (odds ratio 6.06 [associated with a 1 cm increase in LA-ESO], 95% confidence interval [CI] 1.90-19.25; p=0.002). After adjusting for age, BMI and LA area, the association remained significant (odds ratio 5.30, 95% CI 1.39-20.24; p=0.015). The assumption of proportional odds was satisfied. Given that it was a registry study of imbalanced data, propensity scores were estimated in a logistic regression model by setting 75% percentile of LA-ESO as the outcome variable and age, BMI, LA area, and patient characteristics (gender, hypertension, hyperlipidemia, diabetes mellitus, CAD, congestive heart failure, and
hypothyroidism) as the covariates. A propensity score-adjusted multivariable logistic regression was then performed. The obtained odds ratio was 6.17 (95% CI 1.60-23.85; p=0.008).

To offset missing data of LA-ESO and BMI in the small sample size, overall mean imputation was applied to get a complete set of data. For adjusted ordinal logistic regression, with the overall mean imputation the odds ratio turned out to be 5.09 (95% CI 1.51-17.19; p=0.009).

**Discussion:**

In an imaging analysis of 169 patients with cardiac CT, we found a significant, direct, relationship between AF burden and the thickness of the posterior peri-atrial fat pad between the esophagus and the left atrium. Furthermore, this relationship remained statistically significant after adjusting for BMI, age, LA-area, and propensity score.

AF has been associated with obesity (17), as well as elevated C-reactive protein levels (5-9), a measure of systemic inflammation. Left atrial biopsies from patients with lone AF have shown inflammatory cells (10). Obesity has been related to pericardial fat deposits (13). A similar relationship between obesity, epicardial fat, and inflammation has been described for coronary artery disease. It is increasingly recognized that distinct fat depots (such as subcutaneous and visceral fat depots) differ in metabolic activity and in the pro-inflammatory mediators secreted (21). Epicardial adipose tissue is a form of visceral adipose tissue located between the myocardium and the parietal pericardium that shares a common embryonic origin with intra-abdominal adiposity, a fat depot believed to play a role in metabolic syndrome (15, 21-23). Epicardial fat is a source of several inflammatory mediators, including interleukin-1β, interleukin-6, tumor necrosis factor-α, and monocyte chemoattractant protein-1. Paracrine
interactions of these cytokines and mediators contribute to peri-vascular inflammation and the
development of CAD (12-16, 21-23). As left atrial biopsies from patients with AF have shown
evidence of inflammatory cells in the atrial tissue, and a local inflammatory response may have a
role in the development of AF (11), we hypothesized that peri-atrial fat may be associated with
AF, perhaps as a promoter of AF persistence or reflective of the inflammatory changes
associated with AF.

It is interesting that only the LA-ESO (esophageal) peri-atrial fat was found to be
associated with AF burden in our study. Triggers that contribute to the initiation of AF are
located in the pulmonary vein ostia (24). The esophagus follows a course along the posterior wall
of the left atria and is in close anatomical proximity to the pulmonary vein ostia (25-26). Local
inflammatory mediators produced by the peri-atrial epicardial fat in the LA posterior wall may
promote the activation of ectopic foci in the pulmonary vein ostia. Moreover, posterior
pericardiectomy during cardiac surgery has been associated with reduction in postoperative AF
(27-30). This may in part be due to removal of the posterior esophageal pericardial fat pad.

While epicardial adipose tissue is considered to be pro-inflammatory and is associated
with metabolic syndrome and CAD, not all epicardial fat pads are similar. The heart is reported
to have mainly 3 epicardial fat pads with parasympathetic ganglia: a fat pad on the anterior
surface of the atria located between the aorta and the right pulmonary artery, a fat pad between
the inferior vena-cava and left atrium, and one between the superior vena-cava and right atrium
(31). Reports about the impact of surgical preservation of the anterior fat pad between the aorta
and right pulmonary artery on post-operative AF have had conflicting results (31). Epicardial fat
pad ablation in canine models did not suppress AF inducibility in the long term (32). Nevertheless, in this study, only LA-ESO, which has not been characterized as having abundant
parasympathetic ganglia, was significantly associated with AF. Of interest, the LA-TA, LA-PA, and RS fat pads were not associated with AF in our study population and rather appear to decrease in size with AF burden, but this did not achieve statistical significance. It is possible that, in a larger study, the trend toward thicker non-posterior fat pads in the no AF group might reach statistical significance or correlate with the higher prevalence of CAD in the no AF group. CAD has been associated with epicardial fat, and the non-posterior fat pads are likely in closer proximity to the coronary arteries, rather than the pulmonary veins.

Histological analysis and molecular identification of inflammatory markers may be necessary in future studies to better explain this association and to determine whether targeting left atrial adiposity is rational as a therapeutic goal. Preliminary data suggest a role for statins in the primary and secondary prevention of AF, possibly due to their anti-inflammatory effects (33-34). Although speculative, it is possible that patients with more posterior peri-atrial fat, such as patients with persistent AF, might derive more benefit from anti-inflammatory therapy to help reduce AF burden.

**Limitations**: The AF and no AF groups may not represent all patients with and without AF. AF patients in this study were younger than the typical AF population which may lead to a lower prevalence of certain age-associated medical conditions such as HTN. This may limit the applicability of our results to all AF patients. Similarly, patients in the no AF group were generally referred for evaluation for CAD and thus had a larger prevalence of CAD and associated medical conditions. This may have contributed to the trend toward thicker non-posterior left atrial fat thicknesses observed in the no AF group, as previous literature suggests a relationship between coronary atherosclerotic disease and pericardial fat. Optimally, a matched control without AF and without CAD should be used; however, this would require a prospective
enrollment of such patients in a controlled trial. Nonetheless, propensity score-adjusted logistic regression was performed to adjust for imbalances of the registry data.

Although blinding was potentially limited by differences in slice thickness, and labeling for studies that assessed CAD, the CT reading was blinded to AF status. Although thickness of peri-atrial fat along the atrial wall is variable (25-26), the mid LA was used as a landmark to measure peri-atrial fat using the shortest distance to the esophagus, pulmonary artery, and thoracic aorta. A similar method was also applied to retrosternal fat measurements, using the ostium of the right coronary artery as the landmark.

Our method of quantifying fat has limitations as it is unclear if the epicardial fat thicknesses based on a short axis view at the mid left atrium is representative of overall LA epicardial fat. A better assessment of peri-atrial and retrosternal fat may have been possible if an automated method to measure the peri-atrial fat volume were available. While such analytic approaches have been described to analyze epicardial fat surrounding the entire heart (12-13), we are currently unaware of software allowing limited assessment of peri-atrial fat burden. Future software development may allow future studies to include volumetric assessments of peri-atrial fat. Nevertheless, given the possible specific significance found in this study of LA-ESO fat, the posteriorly located fat pad located near the pulmonary veins where AF triggers are located, focal fat quantification may continue to be of interest, in addition to global periatrial fat volumes. Volumetric assessments may also overcome variability in posterior LA fat measurements that may be related to dynamic changes in esophageal movement relative to the posterior LA wall.

**Implications:** In our study, we investigated whether or not LA epicardial fat is associated with atrial fibrillation. Our study suggests that the thickness of the posterior epicardial fat pad between the LA and the esophagus (LA-ESO), which can easily be measured using cardiac CT,
is associated with an increased AF burden independent of the known AF risk factors of age, BMI, and LA size. This may be explained in part by its proximity to the pulmonary vein ostia which have known contributions to AF pathogenesis. These findings have potential implications for better understanding of AF pathogenesis. Inflammation and inflammatory states have been not only associated with AF duration and persistence, but also with the future development of AF in patients without prior history of AF. While further studies are needed to determine the inflammatory role of the posterior LA epicardial fat pad and its cause/effect relationship with AF, measurement of LA-ESO thickness during cardiac CT may prove to have a similar role as other routinely measured inflammatory markers in relation to AF.

Conclusion:
Increased posterior left atrial-esophageal fat pad thickness appears to be associated with increased AF persistence, independent of age, BMI, and LA-area. This first study to describe an association between LA pericardial fat and AF is hypothesis generating but does not define causal connections. Future investigations are needed to further clarify the role of LA pericardial fat in AF and to study the potential inflammatory role of posterior peri-atrial adiposity at a microscopic and molecular level.

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Conflict of Interest Disclosures: None
References:


Table 1: Patient characteristics and biomarkers by AF burden

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th>No AF</th>
<th>Paroxysmal AF</th>
<th>Persistent AF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (%)</strong></td>
<td>169</td>
<td>73 (43.2)</td>
<td>60 (35.5)</td>
<td>36 (21.3)</td>
</tr>
<tr>
<td><strong>Age, years, mean ± SD †</strong></td>
<td>54.6 ± 13.2</td>
<td>50.1 ± 12.8</td>
<td>58.1 ± 12.4</td>
<td>58.0 ± 12.9</td>
</tr>
<tr>
<td><strong>Female, N (%)</strong></td>
<td>59 (34.9)</td>
<td>30 (41.1)</td>
<td>18 (30.0)</td>
<td>11 (30.6)</td>
</tr>
<tr>
<td><strong>BMI, kg/m², mean ± SD (N)</strong></td>
<td>29.2 ± 6.1 (140)</td>
<td>29.2 ± 5.9 (47)</td>
<td>27.8 ± 6.1 (59)</td>
<td>31.4 ± 6.0 (34)</td>
</tr>
<tr>
<td><strong>Comorbidities, N (%) ‡</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD †</td>
<td>26 (15.4)</td>
<td>19 (26.0)</td>
<td>6 (10.0)</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>HTN</td>
<td>66 (42.9)</td>
<td>23 (39.7)</td>
<td>25 (41.7)</td>
<td>18 (50.0)</td>
</tr>
<tr>
<td>HPL</td>
<td>64 (41.6)</td>
<td>20 (34.5)</td>
<td>26 (43.3)</td>
<td>18 (50.0)</td>
</tr>
<tr>
<td>DM</td>
<td>11 (7.1)</td>
<td>5 (8.6)</td>
<td>6 (10.0)</td>
<td>0</td>
</tr>
<tr>
<td>CHF</td>
<td>9 (5.8)</td>
<td>2 (3.4)</td>
<td>4 (6.7)</td>
<td>3 (8.3)</td>
</tr>
<tr>
<td>CKD</td>
<td>3 (1.9)</td>
<td>1 (1.7)</td>
<td>2 (3.3)</td>
<td>0</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>16 (10.4)</td>
<td>5 (8.6)</td>
<td>7 (11.7)</td>
<td>4 (11.1)</td>
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<tr>
<td>Hyperthyroidism</td>
<td>3 (1.9)</td>
<td>0</td>
<td>2 (3.3)</td>
<td>1 (2.8)</td>
</tr>
</tbody>
</table>

* SD= standard deviation, AF= atrial fibrillation, BMI= body mass index, CAD= coronary artery disease, CHF= congestive heart failure, CKD= chronic kidney disease, DM= diabetes mellitus, HPL= hyperlipidemia, HTN= hypertension.

†p<0.015 when comparing age of no AF vs paroxysmal AF (p=0.001) and no AF vs persistent AF (p=0.007), and prevalence of CAD in no AF vs persistent AF (p=0.003). All other comparisons had p>0.015. Bonferroni adjustment was applied in the multiple comparisons.

‡ 15 patients had incomplete documentation of their past medical history in their medical records (excluding AF or CAD which were available in the CT report) and were treated as missing in terms of comorbidities.
Table 2: Left atrial size, Peri-atrial and retrosternal fat thickness*

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th>No AF</th>
<th>Paroxysmal AF</th>
<th>Persistent AF</th>
</tr>
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<tbody>
<tr>
<td><strong>Peri-atrial fat thickness (cm)</strong></td>
<td></td>
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<tr>
<td>LA-PA, cm, median (IQR) (N)</td>
<td>0.65 (0.44, 0.94) (157)</td>
<td>0.68 (0.44, 0.94) (68)</td>
<td>0.66 (0.45, 0.96) (56)</td>
<td>0.55 (0.41, 0.72) (33)</td>
</tr>
<tr>
<td>LA-ESO, cm, median (IQR) (N)</td>
<td>0.40 (0.25, 0.59) (139)</td>
<td>0.34 (0.21, 0.52) (56)</td>
<td>0.39 (0.27, 0.54) (55)</td>
<td>0.56 (0.40, 0.69) (28)</td>
</tr>
<tr>
<td>LA-TA, cm, median (IQR) (N)</td>
<td>0.58 (0.39, 0.90) (148)</td>
<td>0.53 (0.39, 0.95) (62)</td>
<td>0.59 (0.41, 0.89) (55)</td>
<td>0.61 (0.39, 0.74) (31)</td>
</tr>
<tr>
<td><strong>Retro-sternal fat, cm, mean ± SD (N)</strong></td>
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<tr>
<td>0.70 ± 0.42 (164)</td>
<td>0.78 ± 0.49 (72)</td>
<td>0.64 ± 0.32 (57)</td>
<td>0.64 ± 0.36 (35)</td>
<td></td>
</tr>
<tr>
<td><strong>LA-Area, cm², mean ± SD (N)†</strong></td>
<td>21.2 ± 6.76 (169)</td>
<td>18.6 ± 4.45 (73)</td>
<td>21.6 ± 6.97 (60)</td>
<td>25.8 ± 7.77 (36)</td>
</tr>
</tbody>
</table>

AF= atrial fibrillation, LA-ESO= epicardial fat located between mid left atrium and esophagus, LA-PA= epicardial fat located between mid left atrium and pulmonary artery, LA-TA= epicardial fat located between mid left atrium and thoracic aorta, RS= retrosternal fat at the level of RCA ostium, IQR= interquartile range, SD= standard deviation.

† p<0.015 when comparing LA-ESO in no AF vs persistent AF (p=0.003) and paroxysmal AF vs persistent AF (p=0.011), and LA-Area in no AF vs persistent AF (p<0.001) and paroxysmal AF vs persistent AF (p=0.004). All other comparisons had p>0.015. Bonferroni adjustment was applied in the multiple comparisons.
**Figure Legend:**

**Figure 1:** Reconstruction of the short axis view

Standard 2-(right upper figure) and 4-chamber (left lower figure) views are constructed first. The short axis view (left upper figure) was reconstructed as a plane perpendicular to the long axis of these two views at the level of the mid left atrium as indicated by the red line.

**Figure 2:** The heart in the short axis view at the level of the mid LA

In this view, the thickness of the epicardial fat can be demonstrated between the LA and three anatomical landmarks: esophagus, main pulmonary artery and descending thoracic aorta. Actual measurements were taken after window optimization for each location.

PA=main pulmonary artery, LA =left atrium, ASC AO =ascending aorta, DES AO =descending aorta, ESO =esophagus, LA-PA=peri-atrial epicardial fat located between mid left atrium and pulmonary artery, LAESO= peri-atrial epicardial fat located between mid left atrium and esophagus, LATA=peri-atrial epicardial fat located between mid left atrium and thoracic aorta

Orientation Cube: A=anterior, L=left, F=feet

**Figure 3:** Magnified short-axis view of the peri-atrial fat pad between the esophagus and mid LA demonstrating measurement of the LA-ESO fat pad thickness.

There are 5 different layers identifiable starting from the left atrial cavity to the esophageal lumen in order: the left atrial cavity with radiocontrast is most radiodense, a thin LA wall that is less radiodense than the LA cavity, a relatively radiolucent layer of epicardial fat, the esophageal muscle wall, and the esophageal lumen with the radiodensity of air.

DES AO=descending aorta, ESO =esophagus, LA =left atrium, LAESO=peri-atrial epicardial fat located between mid left atrium and esophagus

Orientation Cube: A=anterior, L=left, F=feet

**Figure 4:** The heart in the axial view at the level of the RCA ostium
Measurement of the retrosternal fat (RS) was determined in this view as the shortest distance (indicated by the white double arrow) between the ventricular wall and the parietal pericardium at the level of the RCA ostium (indicated by the anteriorly directed retrosternal white arrow).

Orientation Cube: F=feet

**Figure 5:** Relationship of mean epicardial fat thickness between the esophagus and the mid-left atrium and atrial fibrillation burden

There is a trend towards increasing epicardial fat thickness between the esophagus and the mid-left atrium (LA-ESO) in patients with higher burden of atrial fibrillation (AF). Patients with persistent atrial fibrillation have a significantly thicker mean LA-ESO fat pad than patients with no AF or with paroxysmal AF.
Left Atrial Epicardial Adiposity and Atrial Fibrillation
Omar Batal, Paul Schoenhagen, Mingyuan Shao, AlaEddin Ayyad, David R. VanWagoner, Sandra S. Halliburton, Patrick J. Tchou and Mina K. Chung

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