

Commentary on: Pericardial Fat is Independently Associated with Human Atrial Fibrillation by Al Chekakie et al.

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Introduction

Obesity is an established risk factor for atrial fibrillation (AF).¹ In fact, it has been reported that the increasing prevalence of obesity in the United States could account for up to 60 % of the increasing incidence of age and sex adjusted AF.² Adipose tissue has been shown to be highly metabolically active and secretes several proinflammatory mediators; however, different fat depots differ in metabolic and inflammatory activity.³ Pericardial fat produces several inflammatory cytokines and is believed to play an important role in cardiovascular pathology, and particularly in coronary artery disease.⁴⁻⁷ There exists increasing evidence that links AF and inflammation. The concentration of serum C-reactive protein (CRP), a marker of systemic inflammation, is increased in patients with AF, and has been associated with the development of new AF as well as AF persistence.⁸⁻⁹ Given the association of AF with central obesity and systemic inflammation, investigating the role of pericardial fat, a local fat depot with high inflammatory potential, is of interest. Al Chekakie et al.¹⁰ investigated the association of atrial fibrillation and pericardial fat.

Study Summary

Al Chekakie et al.¹⁰ test the hypothesis that atrial

fibrillation is associated with pericardial fat. The study population consisted of consecutive patients who underwent cardiac CT for AF ablation (N=197) or to investigate potential cardiac symptoms with no history of AF (N=76). Pericardial fat volume was determined by manually tracing the pericardium and using a threshold setting of -190 to -30 Hounsfield units to identify adipose tissue.

The results show that pericardial fat volume was significantly larger in patients with AF as compared to patients in sinus rhythm (101.6 ± 44.1 vs 76.1 ± 36.3 ml, $p < 0.001$). Furthermore, there was a step wise increase of pericardial fat volume with increasing AF burden: 76.1 ± 36.3 ml in normal sinus rhythm versus 93.9 ± 39.1 ml in paroxysmal AF and 115.4 ± 49.3 ml in persistent AF, $p < 0.001$. Regression analysis showed that pericardial fat volume was found to be independently associated with atrial fibrillation (odds ratio 1.13; 95% confidence interval: 1.03 to 1.24, $p = 0.01$) and was also found to be associated with both paroxysmal (odds ratio 1.11; 95% confidence interval: 1.01 to 1.23, $p = 0.04$) and persistent AF (odds ratio 1.18; 95% confidence interval: 1.05 to 1.33, $p = 0.004$) after adjusting for age, sex, body mass index, hypertension, diabetes mellitus, valvular heart disease, left ventricular ejection fraction, and left atrial enlargement.

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Clinical Interpretation and Implications

Obesity is an important risk factor of atrial fibrillation, and has been associated with several cardiovascular comorbidities which have been shown to increase AF risk such as hypertension, diabetes mellitus, congestive heart failure, and obstructive sleep apnea.¹ Visceral obesity, and particularly pericardial fat, has been the subject of several recent studies investigating the association of local fat depots, inflammation, and cardiovascular disease; three of which have looked at the association of pericardial fat and AF.^{4-7, 10-12} In these studies, pericardial fat volume^{10, 12} and posterior left atrial epicardial fat pad thickness¹¹ were associated with atrial fibrillation after adjusting for age, sex, body mass index, comorbid cardiovascular risk factors,¹⁰⁻¹² and left atrial size.¹⁰⁻¹¹ Atrial fibrillation has been associated with inflammation, but the mechanism of this association remains unclear. As pericardial fat is directly contiguous with the atria and has been reported to exert a local inflammatory milieu, this association may provide a mechanistic explanation and contribute to further understanding AF pathogenesis.

The study by Al Chekakie et al.¹⁰ suggests several important clinical implications. Pericardial fat volume was found to be associated with AF independent of left atrial size and independent of other known AF risk factors, and may prove to be an important risk factor for development of AF. However, currently the cause and effect relationship between AF and pericardial fat is not clear, and it would be interesting to prospectively study patients without a prior history of AF who undergo cardiac CT to answer this question.

In this study of AF patients referred for AF ablation, a statistically significant step wise increase in pericardial fat volume was noted with increasing AF burden such that the pericardial fat depot was larger in patients with persistent AF than patients with paroxysmal AF, who in turn had a larger pericardial fat volume than patients in normal sinus rhythm. Prior studies on CRP have shown a similar trend with AF burden and that patients with higher serum CRP tend to have AF recurrence after electrical cardioversion.¹³ Given the inflammatory potential of pericardial fat, it

is possible that patients with a larger pericardial fat volume may have a more malignant substrate, and this suggests a need to investigate the role of pericardial fat and post ablation AF recurrence. Furthermore, investigating the inflammatory milieu of pericardial fat at a molecular level may lead to discovery of potential therapeutic targets in AF management.

The study by Al Chekakie et al.¹⁰ has several limitations that were noted by the authors including selection bias and the potential for uncontrolled confounding. It is interesting to note that the age of included AF patients are younger than the typical AF population and likely represent a subgroup of symptomatic patients despite pharmacological management that required referral for AF ablation. It is unclear if the operators measuring pericardial fat volume were blinded to AF status. Also, the authors did not account for the difference in coronary artery disease among the study groups, given the association of coronary artery disease with pericardial fat volume. In conclusion, this study shows that pericardial fat volume is associated with AF, and suggests the need to further investigate this association which may prove to have important clinical and mechanistic implications.

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