Pericardial fat volume as a predictor of atherosclerosis, stenosis severity and plaque composition in symptomatic and asymptomatic populations - a cardiac CT angiography study

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Introduction

Aim: To evaluate, in asymptomatic and symptomatic population-based cohorts, the relationship between pericardial fat volume (PFV) and indicators of coronary artery disease (CAD), including:

- Presence of atherosclerosis
- Stenosis severity
- Morphological characterization of plaques
- Coronary artery calcium (CAC) score

Background: Coronary CT angiography (CCTA) can provide comprehensive information of the coronary arteries. Previous literature has linked the indicators listed above to the pathogenesis of CAD [1-3]. Visceral fat depots have become an interest in the medical community as research continues to show that BMI is insufficient at predicting cardiometabolic risk [4]. Particularly, CCTA is ideal for calculating the pericardial fat volume (PFV) because of its high spatial resolution and volume coverage; however, the relationship of PFV to CAD has been controversial [5-7]. Pericardial fat may have both a paracrine effect through releasing proatherogenic inflammatory mediators (like IL-1β, IL-6, MCP-1 and TNF-α) as well as a mechanical effect by increasing vascular stiffness [4, 7]. One study found that pericardial fat was a working measure of coronary plaques and was more highly associated with the development of CAD than waist circumference [7]. A study conducted using the Framingham Heart Study population opposed this and concluded that though pericardial fat is correlated with cardiovascular magnetic resonance measures (LV mass, LV end-diastolic volume, and left atrial dimension), this correlation is not stronger than other fat stores or proxy measures of adiposity. [8]

Thesis: PFV contributes to the presence of atherosclerosis and indicates the presence of non-calcified plaques with ≥70% occlusion for symptomatic patients. However, PFV cannot indicate the grading of stenosis or the CAC score.

Methods

Population Selection: The CCTA scans of asymptomatic (383) people and symptomatic (551) patients were examined. The symptomatic patients were part of the "Cardiac cT in the treatment of acute Chest pain" (CATCH) trial and were admitted on suspicion of acute coronary syndrome with a normal electrocardiogram and troponins. The asymptomatic cohort was taken randomly from the Copenhagen General Population Study. Patients were excluded due to poor image quality (n=4).

Figure 1: Symptomatic and Asymptomatic Cohort Characteristics

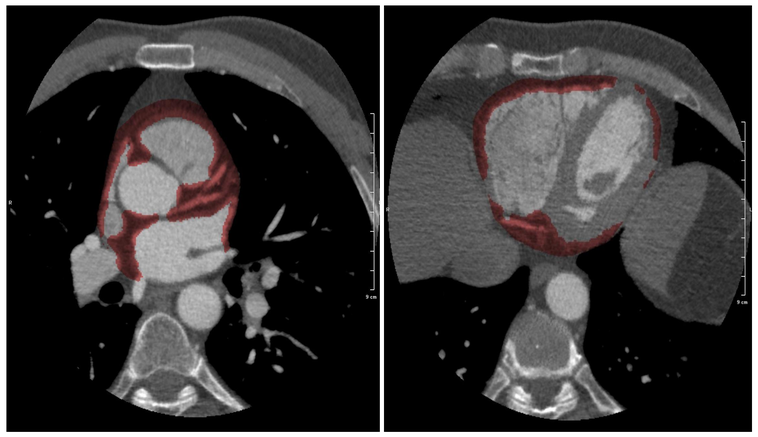
	Symptomatic N=546	Asymptomatic N=430	P-value
BMI, kg/m^2	28±5	25±4	<0.001
Age, years	56±12	61±13	<0.001
Gender, % male	58	51	<0.001
Risk Factors			
Smoking, %	63	54	<0.001
Hypertension, %	41	21	-
Lipid, %	38	-	-
Diabetes mellitus, %	11	4	-
Family History, %	25	-	-
Known CAD, %	14	-	-
Plaque characteristics			
Atherosclerosis Present	305 (59%)	294 (73%)	<0.001
>25% Stenosis	207 (30%)	139 (35%)	<0.001
>50% Stenosis	109 (21%)	72 (18%)	<0.001

Image Acquisition and Analysis: Images were collected using MDCT scan protocol. Stenosis grading was measued using SCCT guidelines. The morphological characteristic was examined on the most severe plaque. Coronary calcium scoring was assessed using the Agatston score method.

Methods

Pericardial Fat Measurement: The pericardial sac was traced at different cross-sections of the heart using the "Sculpt" function with the computer interpolating between the slices. The lowest boundary is where the vessel Post Descending Artery departs and the upper boundary is where the coronary artery Left Main departs. The coronary arteries and other visible vessels were marked with the "Vessel Probe" function and removed from the selected region. The Houndsfield units were limited to the range -190 and -30 and the volume of the region was measured using "Show Volume." Figure 2 shows the PFV highlighted in red.

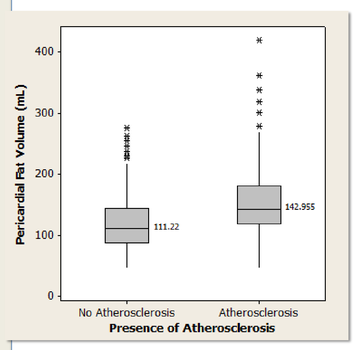
Figure 2: Short Axis View of Pericardial Fat Measurements

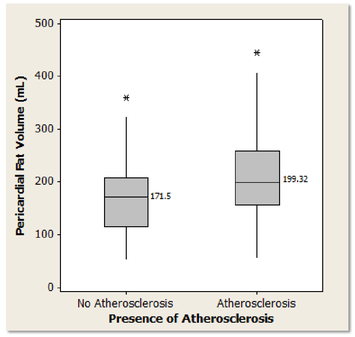


Results

Presence of Atherosclerosis: The symptomatic and asymptomatic cohorts with atherosclerosis had a significantly higher median PFV (142.96 mL and 199.32 mL respectively) compared to those without (111.22 mL and 171.5 mL, with P<0.001. This information is displayed in Figure 3. However, using multivariate linear regression analysis when adjusting for age, gender, and BMI, a larger PFV was significantly associated with atherosclerosis in symptomatic patients (P=0.044). The odds ratio of this regression analysis was 1.01, meaning the odds of having atherosclerosis is greater in individuals with high PFV than for those with low PFV. The concordant percentage was 68.5%. For BMI, P=0.001. This association between PFV and atherosclerosis did not hold for asymptomatic people (P=0.358).

Figure 3: PFV in the Presence and Absence of Atherosclerosis (Left – Symptomatic, Right – Asymptomatic)



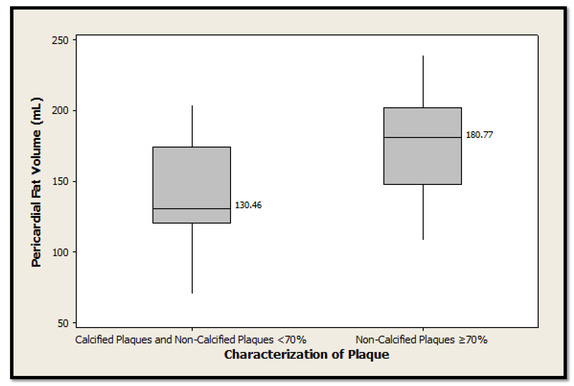


Stenosis Severity: PFV was not a predictor in the symptomatic or asymptomatic populations of mild (≥25%, P=0.158 and P=0.292 respectively), or moderate (≥50%, P=0.087 and P=0.143) coronary artery stenosis.

Results

Morphological Characterization of Plaques: This analysis was conducted on 59 symptomatic patients. The median PFV in patients with non-calcified plaques with ≥70% occlusion (180.77 mL) was significantly higher than the median PFV in patients with calcified plaques or with non-calcified plaques with <70% occlusion (130.46 mL), with P<0.001. These results are displayed in Figure 4. A larger PFV was significantly associated with the presence of non-calcified plaques with ≥70% occlusion (P<0.001). The odds ratio of this regression analysis was 1.03, meaning the odds of having a severe morphological characterization of the plaque for individuals with high PFV is greater than that for individuals with low PFV. The concordant percentage was 78.7%. For BMI, P=0.001. There was no significant association with the presence of non-calcified plaques with ≥50% occlusion (P=0.397).

Figure 4: PFV in Non-Calcified and Calcified Plaques



Coronary Artery Calcium Score: PFV was not a predictor in the symptomatic or asymptomatic populations of CAC (P=0.403, P=0.292 respectively).

Conclusion & Resources

In the present study, it is shown that increased PFV was associated with the presence of atherosclerosis and the presence of non-calcified plaques with ≥70% occlusion, and thus, the risk of developing CAD. When adjusting for other cardiac risk factors, the association was attenuated. The association between PFV and CAD is comparable to the standard measure of adiposity, BMI. However, PFV cannot indicate the degree of stenosis or the CAC score.

The strength of this study was the large population size and the systematic method of measuring pericardial fat. A limitation of the study was the demographic differences between the populations, stemming from the different inclusion/exclusion criteria.

This study has similar results to previous ones, which have found a relationship between CAD risk factors and PFV. [5] What makes this study unique is the finding that PFV is related to the presence of severe, non-calcified plaques. Further studies warrant exploration into the mechanisms by which pericardial fat affects the coronary arteries, specifically, the formation of these non-calcified plaques.

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