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Title: A novel CT-based radiotranscriptomic signature of perivascular fat improves cardiac risk prediction in the SCOT-HEART and CRISP-CT studies

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Topic: 3.2.6. Coronary CT angiography
Short title: Perivascular fat radiomic profile and cardiac risk
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Purpose of the study (600 characters max): Pericoronary fat lipid content changes in response to coronary inflammation, as captured in coronary CT angiography (CCTA) by the dynamic changes of perivascular Fat Attenuation Index. Atherogenesis is also associated with permanent fibrotic and vascular remodelling in the perivascular space. Using artificial intelligence (AI)-powered radiotranscriptomics we developed the perivascular Fat Radiomic Profile (FRP) signature to capture these changes. FRP was then validated in the SCOT-HEART and CRISP-CT studies, where it was found to improve cardiac risk prediction in patients undergoing CCTA.

Main abstract

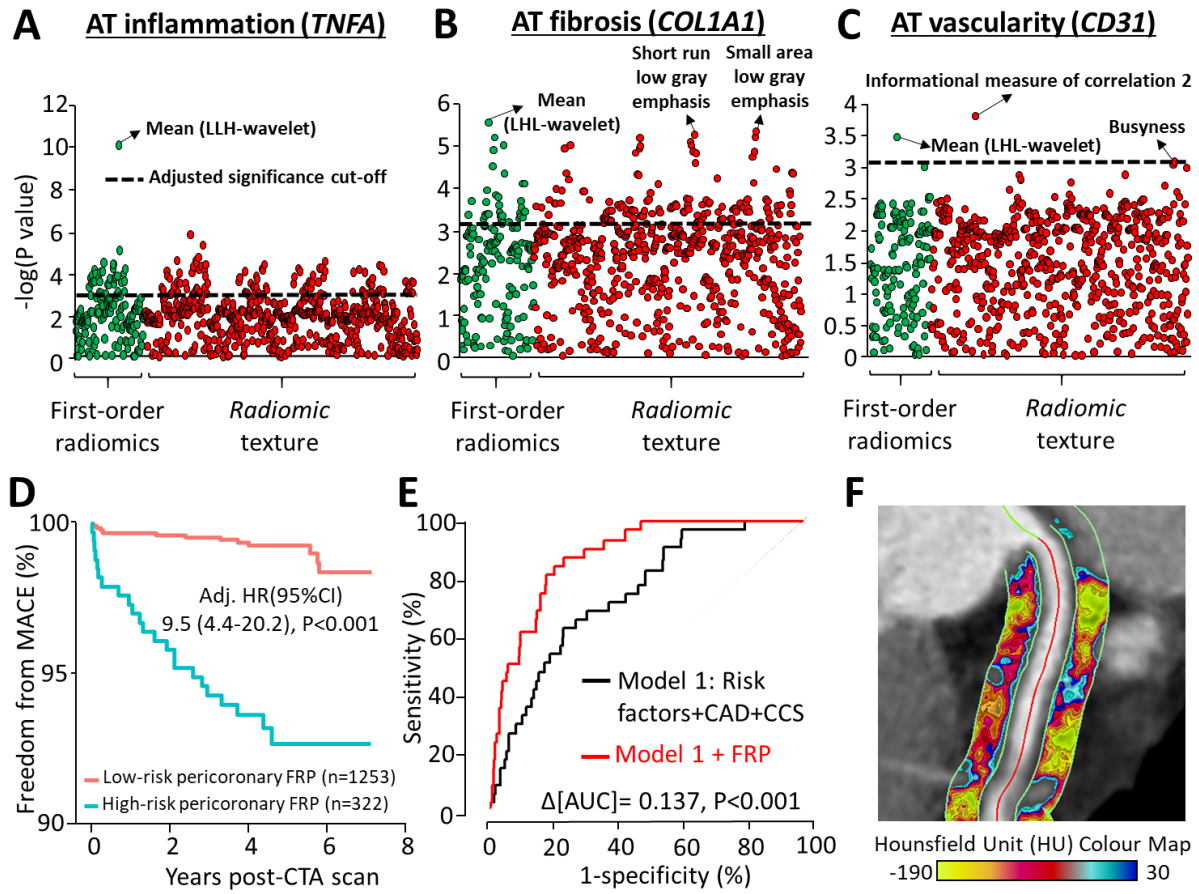
Background: Coronary inflammation induces dynamic changes in the composition of perivascular adipose tissue (PVAT), which are captured by the Fat Attenuation Index on coronary computed tomography angiography (CCTA). However, early atherosclerosis also induces perivascular fat fibrosis and neoangiogenesis, leading to permanent changes in PVAT texture. We hypothesised that by using artificial intelligence (AI)-powered radiotranscriptomics, we could construct a radiomic signature from CCTA images, to describe structural changes in PVAT that will further improving cardiac risk prediction.

Methods: First, we studied the radiotranscriptomic profile of adipose tissue (AT) biopsy specimens obtained from 167 patients undergoing cardiac surgery, exploring the association between radiomic tissue characterization and AT inflammation (*TNFA* gene expression), fibrosis (*COL1A1* gene expression) and vascularity (*CD31* gene expression) (**Arm 1**). We then analysed 1646 radiomic features of PVAT around the right and left coronary artery territories and used machine learning (random forest modelling with five-fold repeated cross-validation) to construct a radiomic signature (Fat Radiomic Profile, FRP) that captures PVAT remodelling and discriminates five-year major adverse cardiac events (MACE) from 1:1 matched controls in the CRISP-CT and SCOT-HEART studies (n=202, **Arm 2**). The performance FRP for major adverse cardiac events (MACE; 5-year cardiac mortality or non-fatal myocardial infarction) was evaluated in 1575 prospectively recruited patients in the SCOT-HEART trial (**Arm 3**). FRP and FAI algorithms are incorporated in the CaRi-HEART platform (Caristo Diagnostics UK).

Results: In Arm 1, wavelet (LLH)-transformed mean AT attenuation (already captured by FAI) was the most sensitive inflammation marker, while radiomic texture was related to AT fibrosis and vascularity (**A-C**). In Arm 2, the FRP signature was constructed based on a machine-learning selected combination of 64 radiomic features measured in coronary PVAT to capture disease-related perivascular remodelling, and discriminated MACE from matched controls (C-statistic[95% CI] 0.77[0.62-0.93]). In Arm 3, subjects with "abnormal" FRP had 9.5-fold higher risk of MACE compared to patients with low FRP, after adjustment for risk factors and calcium score (**D**). Of note, PVAT radiomic mapping significantly improved MACE prediction beyond a traditional CCTA-based risk model (Δ[C-statistic]=0.137, P<0.001), which included age, sex, body mass index, smoking, systolic and diastolic blood pressure, total cholesterol and high-density lipoprotein levels, coronary calcium score and coronary stenosis (**E**). A representative example of perivascular radiomic mapping can be seen in panel **F**.

Conclusions: Coronary atherosclerosis is associated with a shift in the perivascular radiomic texture due to structural changes related to AT adipogenesis, fibrosis and neoangiogenesis. By using artificial intelligence modelling, we constructed a new radiotranscriptomic signature that captures these early signs of disease and improves the prediction of adverse cardiac events in patients undergoing CCTA imaging.

Figure 1.


A
AT inflammation (TNFA)
Mean (LLH-wavelet)
Adjusted significance cut-off
-log(P value)
First-order radiomics
Radiomic texture
B
AT fibrosis (COL1A1)
Mean (LHL-wavelet)
Short run low gray emphasis
Small area low gray emphasis
First-order radiomics
Radiomic texture
C
AT vascularity (CD31)
Informational measure of correlation 2
Mean (LHL-wavelet)
Busyness
First-order radiomics
Radiomic texture
D
Freedom from MACE (%)
Adj. HR(95%CI)
9.5 (4.4-20.2), P<0.001
Low-risk pericoronary FRP (n=1253)
High-risk pericoronary FRP (n=322)
Years post-CTA scan
E
Sensitivity (%)
Model 1: Risk factors+CAD+CCS
Model 1 + FRP
Δ[AUC]= 0.137, P<0.001
1-specificity (%)
F
Hounsfield Unit (HU) Colour Map
-190
30