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CASE SERIES

Highly Inflamed Non-Calcified Coronary Plaques Sealed with Stents in Patients with Zero Calcium Score – a Case Series and Review of the Literature

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ABSTRACT

The modern management of coronary artery disease (CAD) uses coronary computed tomography angiography (CCTA) to enhance plaque evaluation and cardiovascular risk assessment. CCTA identifies high-risk plaques, and the latest CT technologies based on calculation of fat attenuation index (FAI) allow assessment of inflammation at the level of the target coronary artery. We present a series of case studies with chest pain and positive CCTA, in whom a significant stenosis was detected in the left anterior descendent coronary artery, and the existence of high-risk, inflamed plaques was documented even in the context of a zero calcium score. A severe narrowing of the left anterior descending artery, exhibiting the pattern of high-risk anatomy, was associated with a very high inflammation depicted by FAI analysis in all three cases, an association that may be extremely dangerous. In this case series, CCTA examination led to immediate stenting of the obstructive stenosis, sealing the dangerous plaque.

Keywords: non-calcified plaque, calcium score, coronary computed tomography angiography, fat attenuation index, coronary inflammation

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INTRODUCTION

The contemporary approach to managing coronary artery disease (CAD) is characterized by the utilization of cardiovascular risk evaluation tools and the identification of significant arterial obstructions.[1] Cardiac computed tomography angiography (CCTA) stands out as a sophisticated, noninvasive diagnostic modality that renders detailed images of the coronary artery lumens and the associated atherosclerotic plaques.[2] This imaging capability enriches the assessment of plaque burden and morphology, thereby augmenting the understanding of coronary atherosclerosis and refining the prognostication of cardiovascular risk.[3]

The role of cardiac imaging professionals transcends the acquisition of high-resolution cardiac images; it involves meticulous analysis and interpretation of these images to inform therapeutic strategies and patient care plans, with the objective of minimizing the reliance on subsequent diagnostic procedures. The Agatston calcium scoring (CAC) method, applied during non-contrast CCTA examinations, is an established surrogate for quantifying coronary plaque burden and has proven to be a valuable adjunct to traditional risk assessment models. However, it is recognized that plaques with a high calcium score are generally more stable and less likely to cause acute coronary syndromes (ACSs).[4,5] Conversely, a low or non-existent calcium score may not suffice for accurate risk stratification.[6,7] The quantification of unstable plaque components, which pose a greater risk of precipitating clinical events, is an area of active investigation. The Coronary Artery Disease Reporting and Data System (CAD-RADS), introduced in 2016, offers a standardized framework for CAD classification, facilitating its integration into individualized patient management protocols.[8]

The microscopic features of arterial plaques, such as the presence of inflammatory cells, small calcium deposits, fragile fibrous caps, and extensive fatty cores, are known to contribute to the likelihood of plaque disruption and resulting heart attacks.[9] CCTA is capable of identifying these high-risk plaques, which appear as areas of low attenuation due to their noncalcified, lipid-rich composition. Recent advancements in this field of research have indicated that the visual identification of such plaques may be instrumental in predicting the risk of myocardial infarction. Nevertheless, these assessments are inherently subjective and labor-intensive, lacking quantitative precision.[10] Recent technological progress has enabled reproducible and semi-automated quantification of plaque components, thereby enhancing the diagnostic yield of contrast-enhanced CCTA.

Current research endeavors in coronary atherosclerosis are directed towards the identification of biomarkers indicative of coronary inflammation, which bears a significant correlation with plaque instability and the potential for acute cardiovascular incidents. In this context, epicardial and perivascular adipose tissue (PVAT) have been the subject of extensive research over the past decade, recognized both as markers and contributors to coronary inflammation.[11,12] The fat attenuation index (FAI), as measured by CCTA, is advantageous in detecting inflammation within the PVAT, given its independence from coronary calcification and systemic inflammation markers like hs-CRP, as well as its lack of association with coronary lumen stenosis.[13,14]

We present a series of case studies that evaluate whether the assessment of pericoronary inflammation, using FAI technology, can improve the classification of coronary plaques as high risk, in patients with coronary stenoses at CCTA but a zero calcium score. The publication of these cases was agreed by the patients and by the institution where the investigations were performed. All study procedures were performed in accordance with the Declaration of Helsinki.

CASE PRESENTATIONS

CASE 1

A 33-year-old male patient with grade 1 obesity presented reporting chest pain during activities that required moderate effort. He was on medication for high blood pressure and high cholesterol, with no significant family history of heart disease. ECG showed a normal sinus rhythm and no signs of ischemia. A transthoracic echocardiogram (TTE) revealed an ejection fraction of 50% and slight hypokinesis of the interventricular septum. Considering these findings, along with his symptoms and test results, we performed a contrast-enhanced CCTA using a 128-slice scanner (Somatom Definition AS, Siemens, Erlangen). The procedure began with a scan to assess coronary calcium, followed by the injection of an iodine-based contrast agent, dosed according to the patient's body weight. The calcium score was 0; however, the scan revealed significant changes and a narrowing of 80–85% in the proximal segment of the left anterior descending (LAD) artery, produced by a lipid-rich plaque (Figure 1, yellow frame).

The images were sent to Caristo Diagnostics (Oxford, UK) for analysis of the inflammation in the PVAT surrounding the stenotic coronary artery (Figure 1, orange

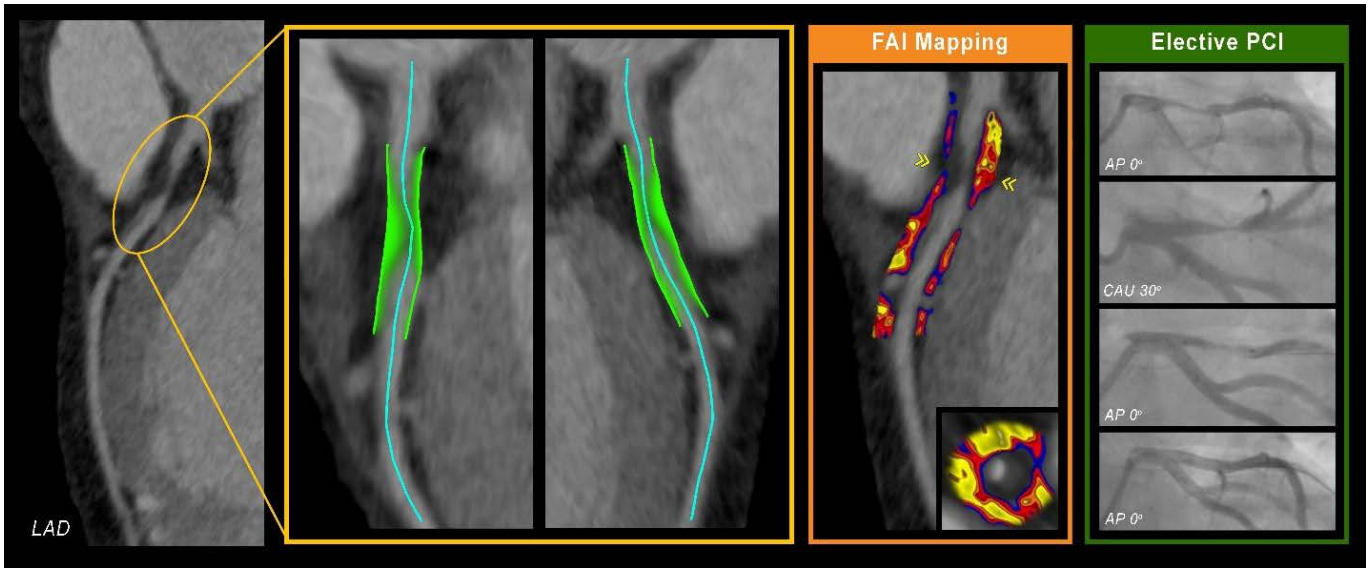

FIGURE 1. In chronological order, the figure includes: (1) Case 1 CCTA scan demonstrating a severe proximal LAD stenosis caused by non-calcified plaque, with two high-risk plaque characteristics present: positive remodeling and low attenuation (on the left side, enclosed by the yellow frame, highlighted by green zones); (2) FAI mapping result of the affected segment, showing an inhomogeneous mix of yellow, red, and blue colors, representing high vascular inflammation (within the orange frame); (3) Elective PCI procedure (enclosed by the green frame).

frame). FAI analysis detected a high level of inflammation in the culprit artery, which indicated a very high-risk plaque (low attenuation, highly inflamed and obstructive). The patient was referred for invasive coronary angiography, which confirmed the critical stenosis of the LAD, and the lesion was stented with good results and a TIMI III postprocedural flow (Figure 1, green frame).

CASE 2

A 59-year-old male patient visited our clinic complaining of chest pain during moderately strenuous activities. His clinical profile was similar with the previously mentioned case, including treatment for hypertension and hypercholesterolemia, and devoid of any notable

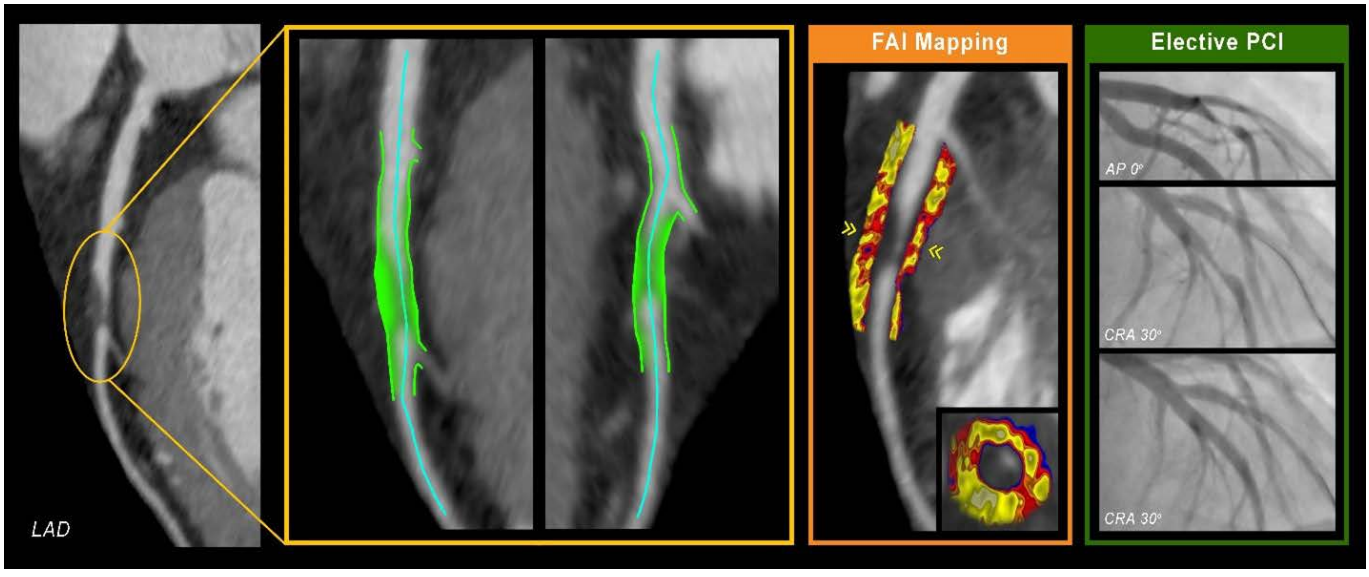

FIGURE 2. (1) Case 2 CCTA scan reveals a severe stenosis in the second segment of the LAD due to a non-calcified plaque, with the same two high-risk plaque characteristics present (enclosed by the yellow frame, highlighted by green zones); (2) FAI mapping of the affected segment displays an uneven mix of yellow, red, and blue colors, indicating high vascular inflammation (within the orange frame); (3) Elective PCI procedure with good results (enclosed by the green frame).

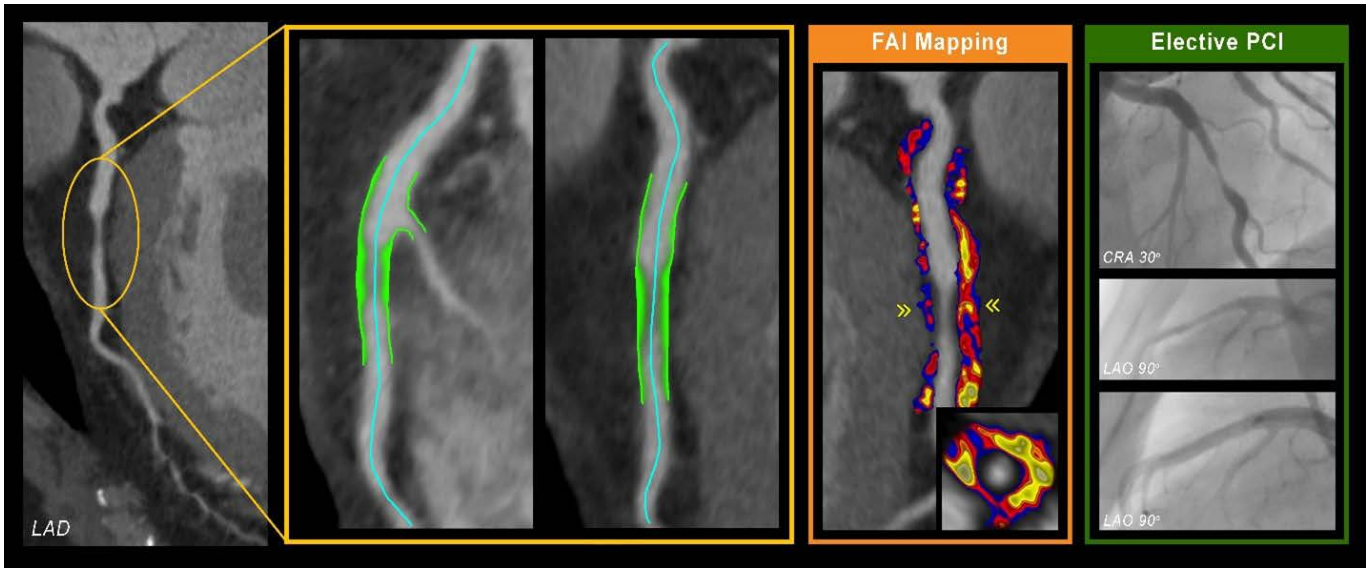

FIGURE 3. (1) Case 3 CCTA scan: Severe LAD stenosis due to non-calcified plaque (yellow frame, green zones); (2) FAI mapping: High vascular inflammation (orange frame); (3) Elective PCI procedure (green frame).

hereditary cardiovascular conditions. His 12-lead ECG was normal, with no evidence of ischemic ST depression. TTE showed a slightly reduced ejection fraction of 47% and mild hypokinesis of the interventricular septum. A contrast-enhanced CCTA was performed on the same day and indicated a zero calcium score, similar to the first case. CCTA showed an 85–90% obstruction in the second segment of the LAD, proximal to the second septal branch, with a high burden of low attenuation plaque (Figure 2, yellow frame).

The acquired images were forwarded to Caristo Diagnosis for FAI analysis, which indicated a high inflammation of the non-calcified plaque (Figure 2, orange frame). Invasive coronary angiography revealed a critical, 85–90% narrowing of the second segment of the LAD, sealed with a coronary stent. The procedure was successful, achieving

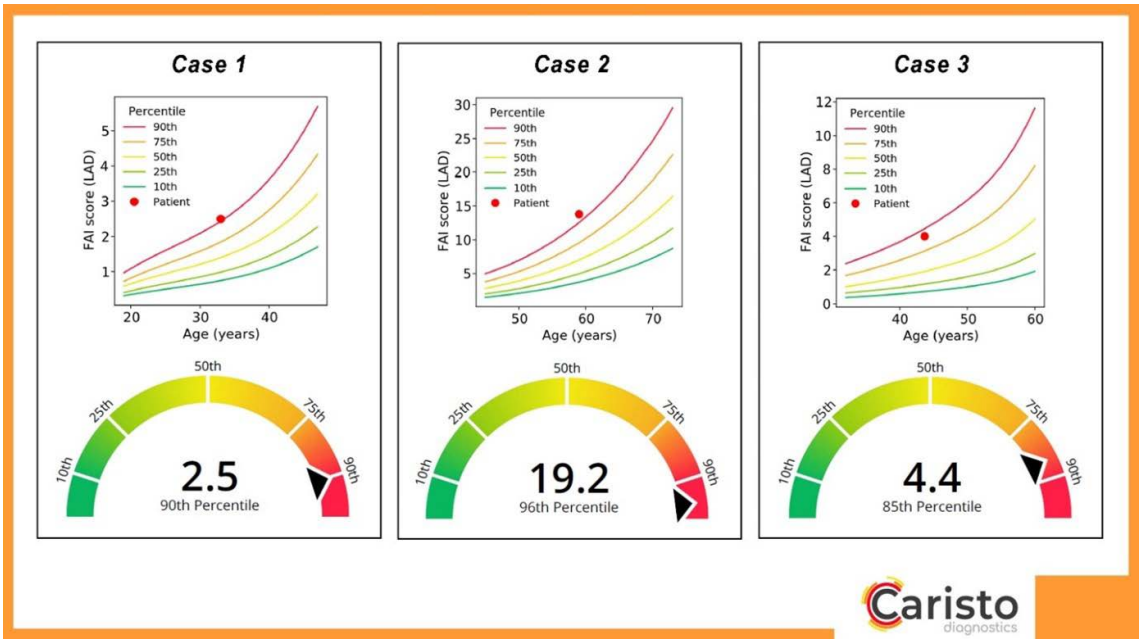

FIGURE 4. PVAT examination findings: FAI score, adjusted relative risk for age and gender, and weighted FAI score of the most inflamed coronary artery

optimal blood flow (TIMI III) to the downstream coronary artery regions (Figure 2, green frame).

CASE 3

The third patient in this case series was a 43-year-old man, who presented with fluctuating episodes of high blood pressure. His medical history resembled that of the two previous patients, involving treatment for both hypertension and hypercholesterolemia, along with grade 1 obesity, but with no significant genetic predisposition to heart disease. His ECG displayed a normal heart rhythm with an intermediate QRS axis and flattened T waves in the V3, V4, DII, and DIII leads. TTE revealed a modest decrease in the ejection fraction to 48% and mild hypokinesis of the inferior and lateral walls of the left ventricle. Contrast-enhanced CCTA showed that similarly to the first two cases, coronary calcium score was 0. However, CCTA identified a 75–80% blockage in the proximal segment of the LAD, caused by a lipid-rich plaque (Figure 3, yellow frame).

FAI assessment indicated a very high level of inflammation in the LAD (Figure 3, orange frame). ICA confirmed the 75–80% obstruction of the LAD in its proximal segment, successfully treated by implantation of a coronary stent, sealing the non-calcified plaque (shown in Figure 3, green frame).

In all three cases, CCTA scans were sent to Caristo Diagnostics (Oxford, UK) for FAI analysis, which revealed a very high inflammation of the stenotic coronary artery (Figure 4). In the first case, a FAI score of 2.5 placed the 33-year-old patient in the 90th percentile for coronary inflammation, well above the norm for their age and sex. Similarly, a second patient, aged 59, had a FAI score of 19.2, ranking in the 96th percentile, near the peak for their demographic. In the third case, aged 43, the FAI score was 4.4, at the 85th percentile for coronary inflammation. All three cases exhibited substantial PVAT inflammation, likely contributing to the formation of non-calcified plaques and potentially playing a role in the development of ACS if not timely intervened in these fortunate instances.

Table 1 summarizes the risk factors, laboratory test results and CCTA features, including the calculated FAI index of inflammation, in the three cases.

TABLE 1. Baseline, risk factors, laboratory and PVAT inflammation parameters for each case

Parameters	Case 1	Case 2	Case 3
Age at time of scan (years)	33	59	43
BMI (kg/m^2)	30.56	25.06	31.22
LVEF (%)	50	47	48
Risk factors			
Hypertension	Yes	Yes	Yes
Hypercholesterolemia	Yes	Yes	Yes
Diabetes	No	No	No
Smoking	No	No	No
Laboratory parameters			
Creatinine (mg/dL)	1.13	0.91	0.87
Total cholesterol (mg/dL)	211	260	172
LDL cholesterol (mg/dL)	103	197	113
Triglycerides (mg/dL)	106	105	107
PVAT inflammation parameters			
FAI (HU)	-68.27	-66.44	-67.38
FAI score	2.50	19.20	4.40
FAI score percentile (%)	90th	96th	85th
Calcium score	0	0	0
CAD-RADS Score	IV A	IV A	IV A
SYNTAX Score	8	5	5
PCI after CCTA	Yes	Yes	Yes
Multi-vessel PCI	No	No	No

BMI, body mass index; LVEF, left ventricular ejection fraction

DISCUSSION

The three cases presented here reveal the existence of high-risk, inflamed plaques even in patients with a zero calcium score. In all three cases, a severe narrowing of the LAD, exhibiting the pattern of high-risk anatomy, was associated with a very high inflammation depicted by FAI analysis. The association between high-risk anatomy, vulnerable plaque, and inflammation may be extremely dangerous and was detected by CCTA. In all three cases, CCTA examination led to immediate stenting of the obstructive stenosis, sealing the dangerous plaque.

Non-calcified plaques occur in as many as 10% of patients with a zero calcium score. Symptomatic individuals with multiple risk factors, such as hypertension and hypercholesterolemia, and a high pretest probability of CAD, may benefit from CCTA evaluations, even when calcium is undetected.[15] Calcium deposits are indicative of stable CAD, whereas ACSs often manifest without detectable coronary calcium. Consequently, calcium presence alone does not suffice for the accurate identification of at-risk coronary plaques.[16] In patients with ACS, plaques of this kind are already advanced, underscoring the need to detect noncalcified plaques that represent an earlier atherosclerotic phase and are more amenable to medical therapy. The early detection of plaques using noninvasive methods can significantly refine treatment approaches. CCTA not only delineates coronary stenoses and blockages but also identifies plaque characteristics and the texture of the adjacent PVAT.[17]

Plaque burden is a strong predictor of cardiovascular events, premised on the understanding that greater plaque volume increases the likelihood of lesion rupture, leading to ACS. The type of plaque is equally critical, with ruptures most frequently occurring in inflamed plaques characterized by a thin fibrous cap and a substantial necrotic core, often in the context of inflamed PVAT.[9,10] Furthermore, FAI mapping via CCTA is beneficial for detecting PVAT inflammation, as it is unaffected by the degree of coronary calcification, systemic inflammation, or the extent of stenosis within the coronary lumen.[11–13] Our recent research, particularly during the COVID pandemic, has demonstrated the utility of these technologies in distinguishing between groups with and without previous SARS-CoV-2 infection.[18,19]

CONCLUSION

In conclusion, high-risk plaques may exist even in patients with zero calcium score and relying solely on CAC scoring for evaluating the risk in CAD may be inadequate. This is evident from the cases with angina and non-calcified plaques, which CAC scoring may overlook. The association of CCTA with PVAT-FAI mapping offers a deeper insight into the extent of plaque accumulation and associated inflammation. This not only improves the identification of plaques that pose a high risk but also aids in tailoring more accurate treatment strategies. CCTA-based assessment of coronary inflammation may detect early signs of high-risk plaques, reconsidering the indication for stenting in order to seal the dangerous plaques.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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