

CASE REPORT

High Inflammation and Coronary Calcification in an Acute Coronary Syndrome Successfully Treated with Cutting Balloon

Emanuel Blîndu^{1,2,3}, Botond–Barna Mátyás^{1,2,3}, Balázs Bajka^{2,3}, Corneliu–Florin Buicu⁴, Monica Chițu^{1,2,3}, Imre Benedek^{1,2,3}

¹ “George Emil Palade” University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania

² Department of Cardiology, Emergency Clinical County Hospital, Târgu Mureș, Romania

³ Center of Advanced Research in Multimodality Cardiac Imaging, CardioMed Medical Center, Târgu Mureș, Romania

⁴ Public Health and Management Department, “George Emil Palade” University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania

ABSTRACT

Complex coronary atherosclerosis may exhibit different phenotypes of coronary plaques, from non-calcified highly vulnerable atheroma to heavily calcified ones. Computed coronary tomography angiography (CCTA) may identify these different phenotypes and the recently introduced CCTA-based techniques for mapping coronary inflammation along the coronary arteries may provide useful additional information on cardiovascular risk. Here we present the case of a 68-year-old male patient with acute coronary syndrome in whom invasive coronary angiography and CCTA revealed a severe three-vessel disease with a heavily calcified lesion. Mapping of the CT fat attenuation index along the coronary arteries identified a high level of coronary inflammation, especially associated with the non-calcified lesions. All lesions were successfully revascularized by implantation of drug-eluting stents. A cutting balloon was used for the lesion identified by CCTA as heavily calcified, followed by stent implantation, with good results. In conclusion, CCTA, in association with novel techniques for mapping coronary inflammation, may represent an extremely useful tool for preparing complex interventions in multivessel diseases, helping preprocedural planning in high-risk patients.

Keywords: fat attenuation index, coronary computed tomography angiography, cutting balloon, pericoronary inflammation

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CORRESPONDENCE

Botond–Barna Mátyás

Str. Gheorghe Marinescu nr. 50

540136 Târgu Mureș, Romania

Tel: +40 265 212 111

Email: mukus44@gmail.com

INTRODUCTION

Atherosclerosis is a persistent inflammatory condition, and the immune system plays a significant part in its advancement. Both systemic and localized inflammation

have a pivotal role in the evolution and advancement of cardiovascular disease (CVD), encompassing a spectrum from endothelial dysfunction to clinical syndromes.¹ It has been demonstrated that inflammatory markers can forecast CVD independently of conventional risk factors. Vari-

Emanuel Blîndu: Str. Gheorghe Marinescu nr. 38, 540139 Târgu Mureș, Romania. Tel: +40 265 208 948, Email: emi.blindu@yahoo.com

Balázs Bajka: Str. Gheorghe Marinescu nr. 50, 540136 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: balazs_bajka@yahoo.com

Corneliu–Florin Buicu: Str. Gheorghe Marinescu nr. 38, 540139 Târgu Mureș, Romania. Tel: +40 265 208 948, Email: florin_buicu@yahoo.com

Monica Chițu: Str. Gheorghe Marinescu nr. 38, 540139 Târgu Mureș, Romania. Tel: +40 265 208 948, Email: iuliachitu@yahoo.com

Imre Benedek: Str. Gheorghe Marinescu nr. 50, 540136 Târgu Mureș, Romania. Tel: +40 265 212 111, Email: imrebenedek@yahoo.com

ous acute and chronic conditions, including established risk factors, psychological stress, autoimmune disorders, microbial and viral infections, and the natural process of aging, can trigger damage and impairment of endothelial function. Endothelial dysfunction caused by inflammation leads to increased permeability to lipoproteins and their accumulation in the endothelium, along with the recruitment of white blood cells and activation of platelets.²

Inflammation in the coronary arteries brings changes in both the structure and function of perivascular adipose tissue (PVAT), resulting in the reduction of adipocyte size and lipid content, accompanied by an elevated aqueous component. As a consequence, PVAT attenuation on computed coronary tomography angiography (CCTA) increases, allowing the noninvasive quantification of coronary inflammation. The mapping of CCTA-derived fat attenuation index (FAI) as a measure of pericoronary inflammation enhances the ability to predict adverse cardiac events beyond traditional imaging-based factors such as the degree of coronary atherosclerosis, coronary calcium score

(CCS), or high-risk plaque characteristics.^{3,4} In addition, several studies have shown that FAI mapping can localize culprit lesions in patients presenting with acute coronary syndromes (ACSs).⁵

In every phase of CAD, there is a degree of calcium deposition within atherosclerotic plaques. While CCS serves as an indicator of an unfavorable prognosis in individuals with CAD and mirrors the burden of atherosclerosis, it does not signify plaque vulnerability.⁶ In the modern era of interventional cardiology, plaques with a high degree of calcification still pose a challenge to percutaneous coronary interventions (PCIs) by disrupting optimal stent expansion, increasing overall risk for procedural complication, and worsening clinical outcomes.⁷

CASE PRESENTATION

We present the case of a 68-year-old male patient with ACS transferred to our hospital from a low-volume interventional center, in whom invasive coronary angiography and

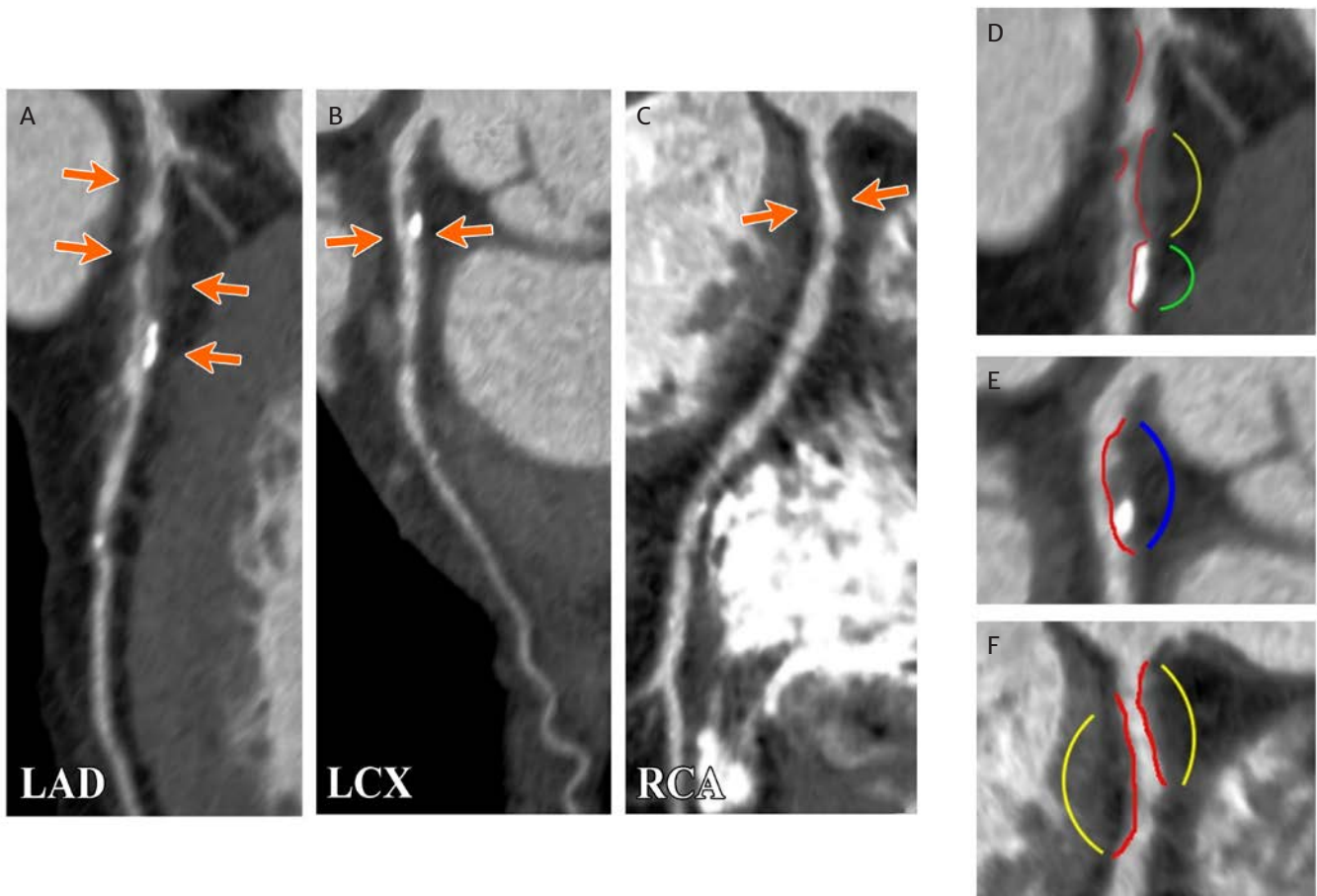


FIGURE 1. CCTA reconstruction of the LAD (A), LCX (B), and RCA (C). D. Area from A; E. Area from B. F. Area from C. Orange arrows, coronary plaques; red lines, the arterial lumen; yellow lines, noncalcified plaque; blue lines, plaque with both calcified and non-calcified contents; green lines, a highly calcified plaque.

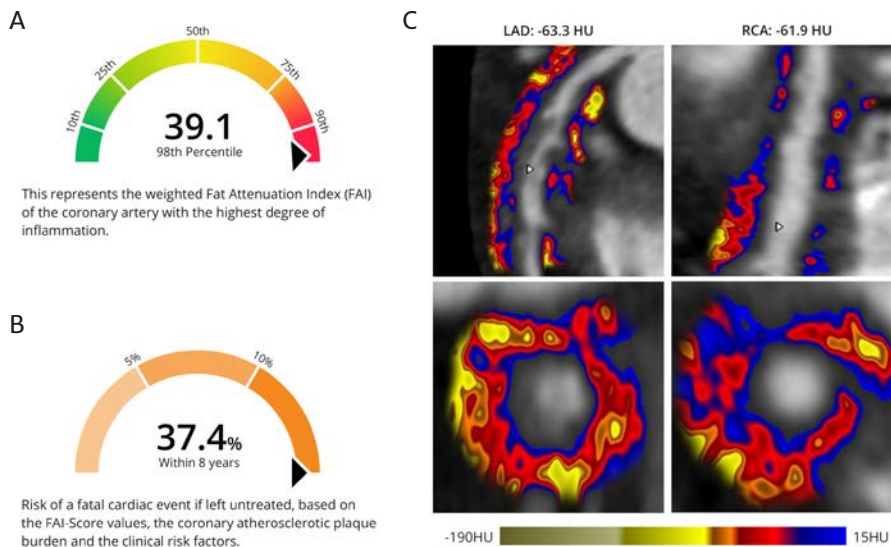
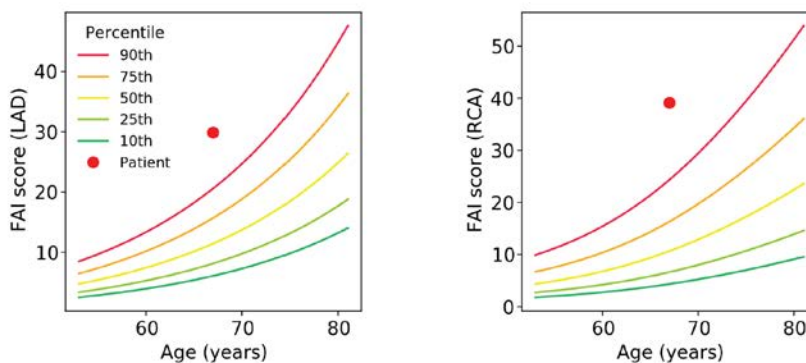


FIGURE 2. Inflammation analysis. **A.** FAI score representing the weighted FAI of the coronary artery with the highest degree of inflammation. **B.** CaRi-Heart risk, the risk of a fatal cardiac event if left untreated, based on the FAI score values, the coronary atherosclerotic plaque burden, and the clinical risk factors, showing a high risk for cardiac events. **C.** Inflammation mapping of LAD and RCA, with hues toward blues representing a higher degree of inflammation.

CCTA revealed a severe three-vessel disease with a heavily calcified lesion and a high level of associated inflammation.

The patient was non-smoker and had no remarkable medical history besides arterial hypertension. The blood lipid panel showed high triglyceride (245 mg/dL) and LDL-cholesterol levels (180 mg/dL). The patient reported that a sudden constrictive chest pain of high intensity started 48 h before presentation. ECG showed negative T waves in V1 to V4 and high-sensitive cardiac troponin I was 932

ng/L (normal value <50 ng/L). The patient underwent urgent invasive coronary angiography, which showed three-vessel disease with heavy calcifications in all vessels. Since the patient was considered to have a medium-risk non-ST-elevation myocardial infarction, in whom the current guidelines do not mandate urgent revascularization, the cardiology team decided to transfer the patient to a high volume-high experience PCI center, the Clinical Emergency County Hospital’s Clinic of Cardiology, where he



Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	29.8	98th percentile
Right Coronary Artery	39.1	98th percentile

FIGURE 3. FAI score percentile placing the patient in the 98th percentile for inflammation adjusted for age and gender

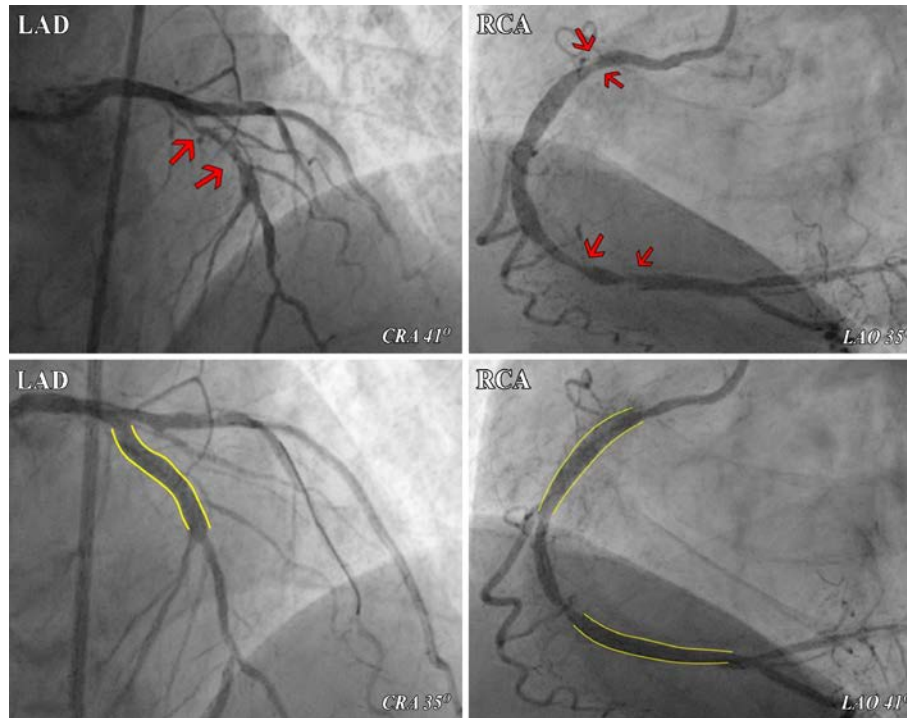


FIGURE 4. Coronary angiography showing severe vascular disease. Red arrows, coronary stenoses on LAD and RCA; yellow lines, sites of stent implantation with minimal residual stenoses

underwent CCTA for preprocedural planning. The CCTA showed moderate stenoses in the left main coronary artery (LMC) and right coronary artery (RCA), and severe stenoses in the left anterior descending (LAD) and circumflex artery (LCX) with a CCS of only 76 and a Coronary Artery Disease Reporting and Data System (CAD-RADS) score of 4. Plaque analysis showed both calcified and non-calcified vulnerable atheroma in the LMC, LAD, and LCX and non-calcified plaques in the RCA (Figure 1).

The acquisition was also sent to Caristo Diagnostics for advanced analysis of inflammation at the level of pericoronary adipose tissue, revealing a high degree of inflammation in both coronary arteries, more expressed in the RCA. FAI index was -63 HU for the LAD and -61 HU for the RCA, with a FAI score of 39.1 and a CaRi-Heart risk of 37.4% (Figure 2). Figure 3 illustrates integrated analysis of the cardiovascular risk of this patient, determined using FAI technology, which placed him in the 98th percentile for coronary inflammation for age and gender, which represents a very high risk for cardiac events.

Following the CCTA identification of calcium distribution in the coronary arteries, revascularization started with the heavily calcified LAD, first preparing the lesion using a cutting balloon. After successful lesion preparation, a drug-eluting stent was implanted with TIMI3 postprocedural flow. In the next step, two drug-eluting

stents were implanted in the RCA (Figure 4). The clinical evolution was favorable, without any complications, and the patient was discharged on double antiplatelet therapy, high-dose statin, ACE inhibitor and beta-blocker. At the 1-month follow-up, the patient was free of events, with minimal loss in ejection fraction and reduction of LDL-C below the target level for high-risk patients (45 mg/dL).

The patient agreed to the publication of his data, and the publication was approved by the institution's ethics committee.

DISCUSSION

Conventional primary prevention models rely on clinical risk factor-based prediction tools, such as the ESC-SCORE, which fail to integrate relevant information regarding the presence, extent, or characteristics of coronary atherosclerosis. While imaging-based measures, such as the CCS, can offer additional risk stratification for cardiovascular issues, it primarily reflects the existence of calcified plaques, which can be influenced by statin treatment. More recent scoring systems for plaque evaluation, such as the CAD-RADS, are available, but they primarily quantify the degree of coronary atherosclerotic disease and do not encompass underlying clinical and biological risk factors, such as coronary inflammation. The new CaRi-Heart

score aims to integrate data regarding clinical risk factors, coronary plaques, and the extent of coronary inflammation, facilitating a personalized assessment of a patient's cardiac risk.³

The case reported here presented to the emergency department with chest pain and no major risk factors, without any cardiovascular event in his history. The patient's low CCS at CCTA indicated a low risk at first sight; however, there were severe stenoses in the coronary arteries, with high CAD-RADS score, that required interventional treatment. At the same time, the patient had a high level of inflammation that contributed to progression of coronary artery disease. Interestingly, in this case the serial non-calcified lesions located in the RCA were associated with a higher level of inflammation, as depicted by FAI analysis, than the highly calcified lesions located in the LAD. This indicates that the degree of calcification is not sufficient to classify a lesion as high risk or not. However, treatment of a highly calcified lesion may be more demanding, requiring special devices, such as cutting balloon in our case. A cutting balloon is a special type of balloon catheter that has small blades on its surface and is used for improving site preparation in highly calcified zones before stent implantation. It may reduce the risk of complications, such as dissections or perforations, that may occur with conventional balloon angioplasty.⁸

Cardiovascular disease prevention involves lifestyle modifications, risk factor reduction, and the use of lipid-lowering therapy. Nevertheless, even with optimal medical treatment and lowered LDL-C levels, individuals displaying atherosclerosis symptoms, particularly of older age or when affected by comorbidities, still face a heightened risk of acute cardiovascular events. Observational studies have indicated that individuals with rheumatic diseases, which are characterized by elevated levels of circulating cytokines, experience a reduced risk of atherosclerotic complications when subjected to specific anti-inflammatory treatments.⁹ Studies have demonstrated that reducing coronary inflammation using specific treatment, such as statins or colchicine, results in fewer cardiac events.^{10,11} Therefore, the detection of high inflammation in the coronary arteries may indicate a higher risk of cardiovascular events and trigger the appropriate intervention for controlling risk factors and reducing atherosclerosis progression.

In our case, CCTA detected a high level of inflammation especially in the non-calcified RCA, in parallel with extensive calcifications in the LCA. We may presume that non-calcified lesions in the right coronary system were more recent than the ones in the left coronary system, and had an accelerated development due to the increased

inflammation. At the same time, our case presented several lesions in different stages of the atherosclerotic process, in the same coronary tree, identifying vulnerable non-calcified, calcified, and mixed plaques. CCTA was extremely helpful for preparing the intervention, providing in one single step the necessary information to perform the complex procedure using the cutting balloon, in parallel with an accurate estimate of lesion-associated risk for all types of lesions.

CONCLUSION

In association with novel techniques for mapping coronary inflammation, CCTA may represent an extremely useful tool for preparing complex interventions in multi-vessel diseases, helping preprocedural planning in high-risk patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Prati F, Marco V, Paoletti G, Albertucci M. Coronary inflammation: why searching, how to identify and treat it. *Eur Heart J Suppl.* 2020;22:E121–E124. doi: 10.1093/eurheartj/suaa076.
2. Menzel A, Samouda H, Dohet F, Loap S, Ellulu MS, Bohn T. Common and Novel Markers for Measuring Inflammation and Oxidative Stress Ex Vivo in Research and Clinical Practice—Which to Use Regarding Disease Outcomes? *Antioxidants (Basel).* 2021;10:414. doi: 10.3390/antiox10030414.
3. Oikonomou EK, Antonopoulos AS, Schottlander D, et al. Standardized measurement of coronary inflammation using cardiovascular computed tomography: integration in clinical care as a prognostic medical device. *Cardiovasc Res.* 2021;117:2677–2690. doi: 10.1093/cvr/cvab286.
4. Mátyás BB, Benedek I, Blöndu E, et al. Elevated FAI Index of Pericoronary Inflammation on Coronary CT Identifies Increased Risk of Coronary Plaque Vulnerability after COVID-19 Infection. *International Journal of Molecular Sciences.* 2023;24:7398. doi: 10.3390/ijms24087398.
5. Klüner LV, Oikonomou EK, Antoniadou C. Assessing Cardiovascular Risk by Using the Fat Attenuation Index in Coronary CT Angiography. *Radiol Cardiothorac Imaging.* 2021;3:e200563. doi: 10.1148/ryct.2021200563.

6. Williams MC, Moss AJ, Dweck M, et al. Coronary Artery Plaque Characteristics Associated With Adverse Outcomes in the SCOT-HEART Study. *J Am Coll Cardiol.* 2019;73:291–301. doi: 10.1016/j.jacc.2018.10.066.
7. Madhavan MV, Tarigopula M, Mintz GS, Maehara A, Stone GW, Généreux P. Coronary artery calcification: pathogenesis and prognostic implications. *J Am Coll Cardiol.* 2014;63:1703–1714. doi: 10.1016/j.jacc.2014.01.017.
8. Mangieri A, Nerla R, Castriota F, et al. Cutting balloon to optimize predilatation for stent implantation: The COPS randomized trial. *Catheter Cardiovasc Interv.* 2023;101:798–805. doi: 10.1002/ccd.30603.
9. Oikonomou EK, Marwan M, Desai MY, et al. Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. *Lancet* 2018;392:929–939. doi: 10.1016/S0140-6736(18)31114-0.
10. Dai X, Yu L, Lu Z, Shen C, Tao X, Zhang J. Serial change of perivascular fat attenuation index after statin treatment: Insights from a coronary CT angiography follow-up study. *Int J Cardiol.* 2020;319:144–149. doi: 10.1016/j.ijcard.2020.06.008.
11. Zhang FS, He QZ, Qin CH, Little PJ, Weng JP, Xu SW. Therapeutic potential of colchicine in cardiovascular medicine: a pharmacological review. *Acta Pharmacol Sin.* 2022;43:2173–2190. doi: 10.1038/s41401-021-00835-w.