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Case Report | Peer-Reviewed Article

Non-invasive and Invasive Pathophysiological, Morphological, and Functional Assessment

Personalized Management of Coronary Atherosclerosis

Apostolos Tsinaridis[a], Marko Gajic[b], Alessandro Candreva[b], Philipp A. Kaufmann[a], Ronny R. Buechel[a], Barbara E. Stähli[b], Andreas A. Giannopoulos[a]

University Hospital of Zurich, Switzerland: [a] Department of Nuclear Medicine, Cardiac Imaging; [b] Department of Cardiology, University Heart Center

Abstract

We present the diagnostic pathway and management of an asymptomatic patient with a solitary, potentially high-risk coronary plaque, utilizing modern and advanced non-invasive and invasive pathophysiological, morphological, and functional assessment. By using coronary computed tomography angiography, computer-based solutions were employed enabling non-invasive understanding of the plaque characteristics and the local and global functional micro-environment. Invasive coronary angiography-based, computational, and wire-free hemodynamic lesion assessment as well as intracoronary imaging with optical coherence tomography were further utilized, allowing for personalized management and guiding coronary revascularization.

Keywords: CCTA; CT-FFR; ESS, OCT; PCAT; QFR

Case Description

A 65-year-old asymptomatic man with a recent diagnosis of dyslipidemia (low-density lipoprotein: 5.8 mmol/l) and prediabetes (HbA1c: 5.9%) without any other cardiovascular risk factors, underwent a routine outpatient cardiology evaluation. Resting electrocardiogram showed a sinus rhythm without any significant de- or repolarization abnormalities. Transthoracic echocardiography revealed normal left ventricle ejection fraction without regional wall motion abnormalities and normal valve function. A bicycle exercise test did not provoke any chest discomfort, however, horizontal ST-segment depression of approximately one millimeter in the inferior leads was observed. A coronary computed tomography angiography (CCTA) was performed to assess for coronary artery disease (CAD).

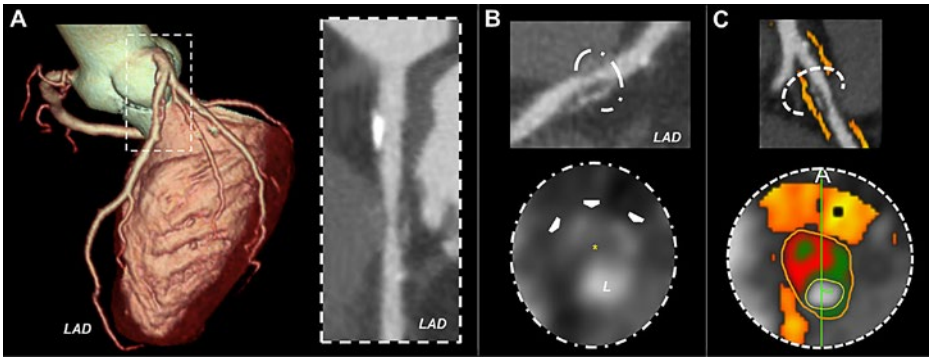

Figure 1: Coronary computed tomography angiography (CCTA) and CCTA advanced morphological analysis. Panel A: 3D rendering of CCTA exam (left) and zoomed multiplanar reconstruction of the proximal left anterior descending coronary artery (LAD) focusing on the mixed plaque causing intermediate obstruction (right). **Panel B:** Multiplanar reconstruction of the proximal LAD (top) with corresponding cross-sectional image of the plaque (bottom) demonstrating a napkin-ring sign. Asterisk: low attenuation core; L: coronary lumen; Arrowheads: circumferential high-attenuation area. **Panel C:** Pericoronary adipose tissue (PCAT) analysis (top), superimposed on the CCTA multiplanar images (orange) and corresponding cross-sectional image (bottom) including the plaque characterization analysis. PCAT: -81 Hounsfield Units; Green: fibrous components; Red: necrotic core pertaining 26% of the entire plaque volume.

CCTA demonstrated mild calcifications (Agatston calcium score of 62) with non-obstructive calcified plaques in the obtuse marginal branch of the circumflex coronary artery and the right coronary artery, and a partially calcific plaque in the proximal left anterior descending artery (LAD) causing intermediate obstruction (~70% luminal diameter stenosis) (fig. 1A). The plaque exhibited anatomical high-risk features, including napkin-ring sign and low plaque attenuation. Advanced imaging analysis assessing the pericoronary adipose tissue of the proximal LAD revealed high values of -81 Hounsfield Units (HU), known to be a marker of vascular inflammation (fig. 1B and C) [1].

Non-invasive functional evaluation of the lesion was performed with computed tomography (CT)-based fractional flow reserve (CT-FFR; X-FFR research prototype, GE Healthcare, Chicago, USA) and CT-based endothelial shear stress (CT-ESS; Fluent, Ansys Inc., Canonsburg, USA) (fig. 2A and B) [2]. A significant hyperemic distal pressure loss was confirmed (CT-FFR = 0.64) indicating potential hemodynamical relevance. Resting blood flow of the LAD was simulated using CCTA and computational fluid dynamics, and the local ESS was calculated (fig. 2B) [3]. The most stenotic plaque region (plaque neck) was characterized by high ESS values (average 4.8 Pa), which are considered to increase the vulnera-

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bility of plaques to rupture or erode. At the distal plaque shoulders, low ESS values (average 0.8 Pa) were observed, associated with inflammation and atherosclerosis progression to a higher-risk phenotype [4].

Based on the clinical and non-invasive anatomical and computational findings, the patient underwent an invasive coronary angiography that confirmed the presence of an intermediate proximal LAD stenosis (fig. 3A). On-site, computational assessment of the hemodynamical significance of the lesion with measurement of the quantitative flow ratio (QFR; Medis QFR, Leiden, The Netherlands) was performed (fig. 3B) and confirmed the hemodynamical significance of the stenosis (QFR of 0.78) [5]. Invasive intracoronary imaging using optical coherence tomography (OCT) measured a minimal lumen area of 2.3 mm^2 and revealed a lipid-rich thick-cap fibroatheroma of the plaque under investigation (fig. 4A). Due to the hemodynamical significance of the lesion, coronary revascularization was performed. Under OCT guidance, enabling appropriate stent sizing and evaluation of the landing zones, the lesion was successfully treated with percutaneous coronary intervention (PCI) and implantation of an everolimus-eluting stent (Synergy Megatron 3.5×28 mm, Boston Scientific, Marlborough, Massachusetts). Post-PCI OCT demonstrated excellent expansion and apposition of the stent (fig. 4B). The patient was discharged with dual antiplatelet therapy (aspirin and ticagrelor) for six months, continuation of statin therapy, and advice for life-style modification.

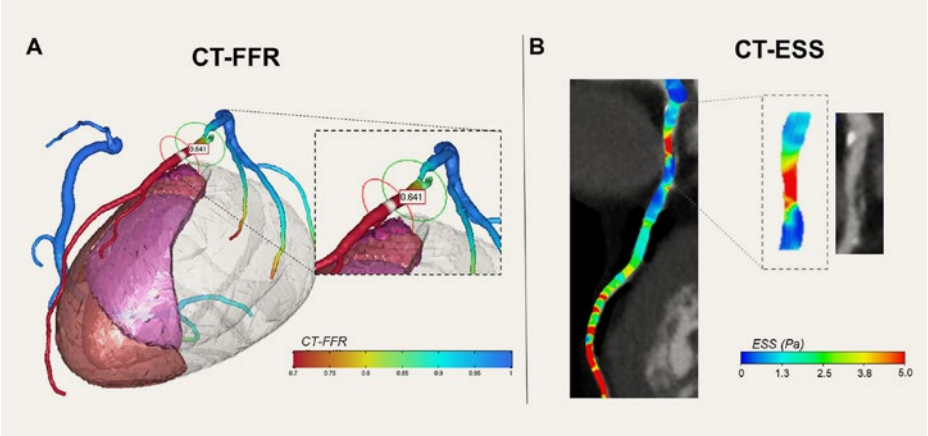

Figure 2: Computed tomography (CT)-based computation flow dynamics. Panel A: CT-based fractional flow reserve (FFR) assessment demonstrating the lesion at the proximal left anterior descending coronary artery to be hemodynamically significant (CT-FFR 0.64). **Panel B:** CT-based endothelial shear stress (ESS) with high ESS values at the neck of the plaque and low ESS values at the distal shoulders of the lesion.

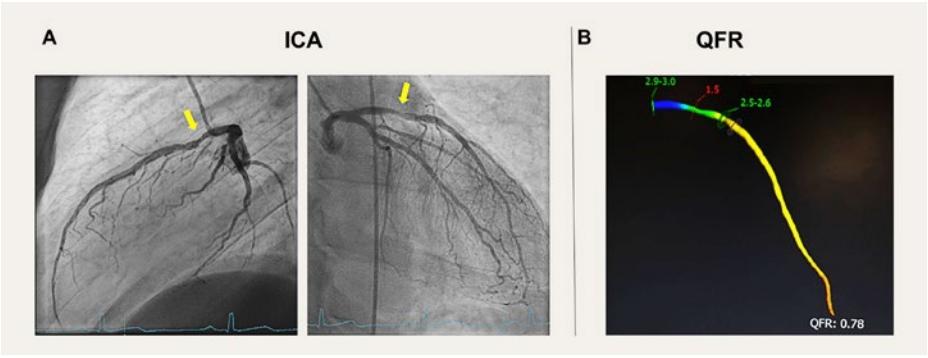

Figure 3: Invasive coronary angiography (ICA) and quantitative flow ratio (QFR). Panel A: Two planes of the invasive coronary angiography with the intermediate lesion in the proximal left anterior descending coronary artery (yellow arrows). **Panel B:** QFR analysis based on the invasive coronary angiograms and computational algorithms demonstrating hemodynamic significance of the lesion (QFR value 0.78).

Discussion

In the presented case, although not reflecting daily routine in our institution, CCTA enabled non-invasive, pathophysiological, morphological, and functional assessment of an intermediate stenosis on a prognostically relevant location with anatomically high-risk morphological features and potential hemodynamic significance. Following CCTA, the patient underwent an invasive investigation that confirmed the physiological significance. PCI was performed with procedural guidance with intracoronary imaging to achieve an optimal result.

CCTA holds a key role in the assessment of patients with suspected CAD and intermediate cardiovascular risk, primarily because of its excellent ability to exclude the presence of significantly obstructive disease. Furthermore, assessment of plaque morphology with CCTA can provide valuable information on the plaque composition and identify high-risk, potentially vulnerable plaques that confer independent incremental predictive value on top of luminal diameter stenosis. Pericoronary fat at-

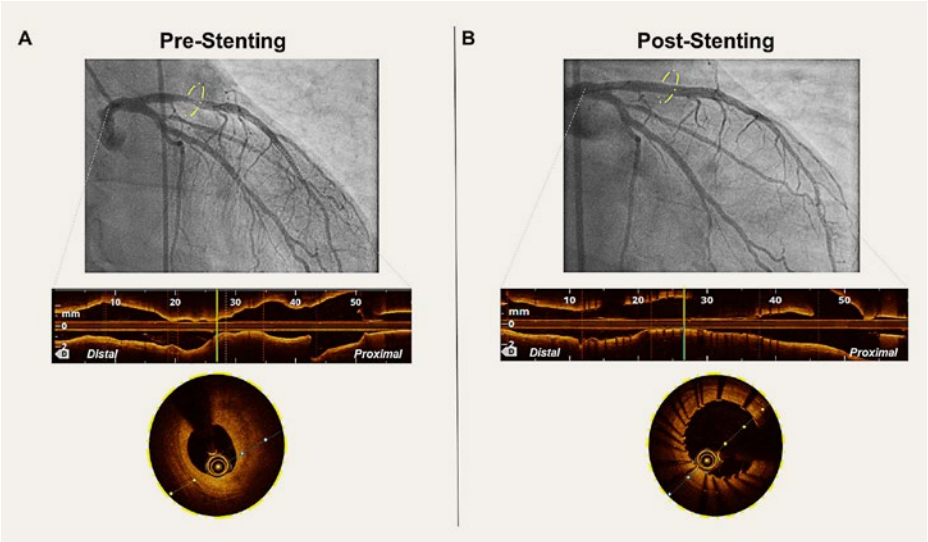

Figure 4: Invasive coronary angiography and optical coherence tomography (OCT) of the proximal left anterior descending coronary artery (LAD) lesion, pre- and post-stenting. Panel A: Pre-interventional coronary angiography (top), OCT longitudinal view (middle), and corresponding OCT cross-sectional view (bottom) of the thick-cap fibroatheroma (yellow). **Panel B:** Post-interventional coronary angiography (top), OCT longitudinal view (middle), and OCT cross-sectional view (bottom) demonstrating an optimal stent expansion and apposition (yellow).

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tenuation has been proven to enhance cardiac risk prediction by providing a quantitative measure of coronary inflammation. High values (cut-off ≥-70.1 HU) have been shown to be predictive of adverse clinical events beyond standard CCTA indices and traditional risk factors.

Recent computational advances have allowed for non-invasive estimation of the functional significance of coronary plaques using CT-based FFR. The methodology has been extensively validated versus its invasive counterpart and is endorsed by European and American guidelines as an add-on exam for intermediate stenosis as an alternative to stress myocardial perfusion testing. Similarly, computational simulations of the resting coronary flow have provided important insights into the pathophysiology of coronary atherosclerosis, mainly through investigation of the local hemodynamic milieu and there are several studies supporting the critical role of local ESS in the initiation and progression of the disease.

Technological advancements of invasive coronary imaging allow for hemodynamic lesion assessment with fast, on-site, computational approaches such as QFR, avoiding the advancement of a coronary guidewire and the induction of hyperemia. These novel, angiography-based methods are emerging as a potential alternative to invasive FFR in selected cases or when access to wire-based physiological indices is limited. Moreover, intracoronary imaging, such as intravascular ultrasound and OCT, is increasingly being used in clinical practice as it allows for a detailed preprocedural lesion assessment, PCI planning, and a high-resolution confirmation of an optimal PCI result.

With the implementation of computational-based software solutions and improvements in intravascular imaging techniques, non-invasive and invasive imaging has significantly improved in the past decades. These novel advancements might open new horizons in the understanding of pathophysiology and could potentially hold a key role in patient-tailored diagnosis and management of chronic coronary syndromes.

Take-home Messages

- CCTA using advanced software can non-invasively provide important pathophysiological, morphological, and functional information on coronary plaques.
- Computer-based evaluation of the hemodynamical significance of coronary lesions on-site and during invasive coronary angiography represents a developing and promising technique.
- Intracoronary imaging is becoming an incremental part of procedural planning and optimization.

Correspondence
Andreas A. Giannopoulos
Department of Nuclear Medicine
Cardiac Imaging
University Hospital of Zurich
Rämistrasse 100
CH-8091 Zürich
andreas.giannopoulos[at]usz.ch

Ethics Statement
Written informed consent was obtained.

Conflict of Interest Statement
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