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CASE REPORT
Coronary intervention

Two birds with one stone: integrated assessment of coronary physiology and plaque vulnerability from a single angiographic view—a case report

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Background Physiology-guided coronary revascularization was shown to improve clinical outcomes in multiple patient subsets, whilst in those presenting with acute coronary syndromes, it seems to be associated with an excess of cardiovascular events. One of the major drawbacks in this setting is the potential deferral of non–flow-limiting but 'vulnerable' coronary plaques.

Case summary A 40-year-old patient presented with a myocardial infarction without ST-segment elevation (NSTEMI). At the invasive coronary angiography (ICA) a sub-occlusive stenosis on his left circumflex artery was detected and treated with percutaneous coronary intervention (PCI). The treatment of a concomitant intermediate eccentric focal stenosis on the right coronary artery (RCA) was deferred after a negative pressure wire–based physiological assessment. The patient was re-admitted 9 months later due to a recurrent NSTEMI, and a severe progression of the deferred RCA lesion was found at the ICA. In retrospect, an angiography-based assessment of physiological severity and plaque vulnerability of the non-culprit RCA stenosis by means of Murray's law–based QFR (μQFR) and radial wall strain (RWS) was performed. At baseline, μQFR value (0.90) corroborated the non-ischaemic findings of wire-based assessment. However, RWS analysis showed a marked hotspot (maximum RWS value 27.7%), indicating the presence of a vulnerable plaque.

Discussion Radial wall strain is a novel biomechanical deformation index derived from coronary angiography. Segments with high RWS are associated with lipid-rich plaques that are prone to progression and plaque rupture. Therefore, the identification of RWS hotspots might potentially improve the risk stratification of non-culprit lesions and empower secondary prevention strategies.

Keywords Plaque vulnerability • Coronary physiology • Acute coronary syndrome • Functional angiography • Adverse cardiac events • Case report

ESC Curriculum 3.1 Coronary artery disease • 3.2 Acute coronary syndrome

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Learning points

- Coronary revascularization decision-making process (deferral vs. stenting) based on intra-coronary physiology is associated with an excess of cardiovascular events in high-risk patients, such as those presenting with acute coronary syndromes, due to the potential deferral of non–flow-limiting but 'vulnerable' non-culprit coronary plaques.
- Radial wall strain (RWS) is a novel biomechanical deformation index that derives plaque mechanical properties from coronary angiography. Segments with high RWS are associated with lipid-rich plaques that are prone to progression and rupture during follow-up.
- The identification of RWS hotspots might potentially improve the risk stratification of non-culprit lesions and empower secondary prevention strategies.

Introduction

Coronary revascularization aims to improve coronary flow and relieve myocardial ischaemia. Invasive wire–based pressure measurements were developed to assess the haemodynamic significance of epicardial coronary artery disease (CAD) and were shown to improve clinical outcomes in multiple patient subsets when used for coronary revascularization guidance or stenting deferral.[1,2] However, in some patient categories, such as those presenting with acute coronary syndromes (ACS) and/or diabetes mellitus, the decision-making process (deferral vs. stenting) based on intra-coronary physiology is associated with an excess of cardiovascular events, compared with patients without such clinical features.[3] Therefore, the evidence in support of physiology-guided revascularisation especially of intermediate non-culprit lesions in ACS patients has been recently questioned.[4] One of the major drawbacks of physiological guidance in the setting of ACS is the potential deferral of non–flow-limiting but 'vulnerable' non-culprit coronary plaques.

Summary figure

2015

Day 1
- Acute onset of chest pain after physical effort
- Emergency department admission
- Blood tests: elevation of troponin I (peak 1046 ng/L)
- Electrocardiogram (EKG) and echocardiogram normal

Day 2 Invasive coronary angiography (ICA):
- Sub-occlusive stenosis on obtuse marginal (OM) branch of the left circumflex artery (LCX)
  → Treated with percutaneous coronary intervention (PCI)
- Intermediate stenosis on the proximal right coronary artery (RCA)
  → Negative fractional flow reserve (FFR) (0.89) and instantaneous wave-free ratio (iFR) (0.93). Medical management

Day 3
- Discharge
- Secondary prevention follow-up programme

2016

Day 1
- Acute onset of chest pain after physical effort
- Emergency department admission
- Blood tests: elevation of troponin I (peak 2850 ng/L)
- EKG and echocardiogram normal

Day 2 ICA:
- Optimal result of the previous PCI to OM branch
- Severe progression of the deferred RCA lesion that has led to a sub-occlusive thrombotic stenosis
  → Treated with PCI

Continued

2022 Retrospective computation of physiology and vulnerability of RCA stenosis based on coronary angiography:
- RWS 27.7%
- μQFR value 0.90

Case report

This case is about a 40-year-old active smoker with known but untreated hypertension and hyperlipidaemia who presented with acute onset of chest pain after physical effort. On admission, the blood tests showed an elevation of troponin I (peak 1046 ng/L), whilst neither ischaemic changes nor regional wall abnormalities were detected on the electrocardiogram and echocardiogram, respectively. At the invasive coronary angiography (ICA), a sub-occlusive stenosis on a large obtuse marginal (OM) branch of the left circumflex artery was detected and successfully treated with percutaneous coronary intervention (PCI) and deployment of a bioresorbable vascular scaffold (BRS; ABSORB 3.5 × 28 mm) as shown in *Figure 1* (Panels A and B). A concomitant intermediate eccentric focal stenosis was present on the proximal right coronary artery (RCA). A pressure wire–based physiological assessment was performed both at rest and under hyperaemia, induced by intra-coronary administration of adenosine (200 μg), with detection of values way above the ischaemic threshold (instantaneous wave-free ratio [iFR] 0.93 and fractional flow reserve [FFR] 0.89) suggesting a safe deferral (*Figure 1C*). The patient was discharged on a daily regimen of dual antiplatelet therapy with clopidogrel 75 mg and acetylsalicylic acid 100 mg for 1 year, together with a high dose of statin (baseline low-density lipoprotein [LDL] cholesterol 141 mg/dL) combined with anti-hypertensive medications. Furthermore, he was enrolled in a secondary prevention dedicated specialized clinic and did achieve optimal blood pressure control and cholesterol levels (LDL 53 mg/dL).

Despite adherence to the prescribed medical therapy, the patient was re-admitted 9 months later due to an acute myocardial infarction without ST-segment elevation, again after a physical effort (peak troponin I 2850 ng/L). At the ICA, an optimal result of the previous PCI with BRS on the OM branch was reported, whilst a severe progression of the deferred RCA lesion had led to a sub-occlusive thrombotic stenosis (*Figure 2A and B*). Another BRS (ABSORB 3.5 × 18 mm) was implanted with good final result (*Figure 2C and D*).

In retrospect, we performed angiography-based assessment of physiological stenosis severity and plaque vulnerability of the non-culprit RCA stenosis, as shown in *Figure 3*. Baseline and follow-up RCA coronary angiograms were analysed using the quantitative flow ratio (QFR) software (AngioPlus Core, version V3, Pulse Medical Technology Inc., Shanghai, China). Murray's law–based QFR (μQFR) and radial wall strain (RWS) were computed based on a single angiographic projection. At baseline, μQFR value (0.90) corroborated the

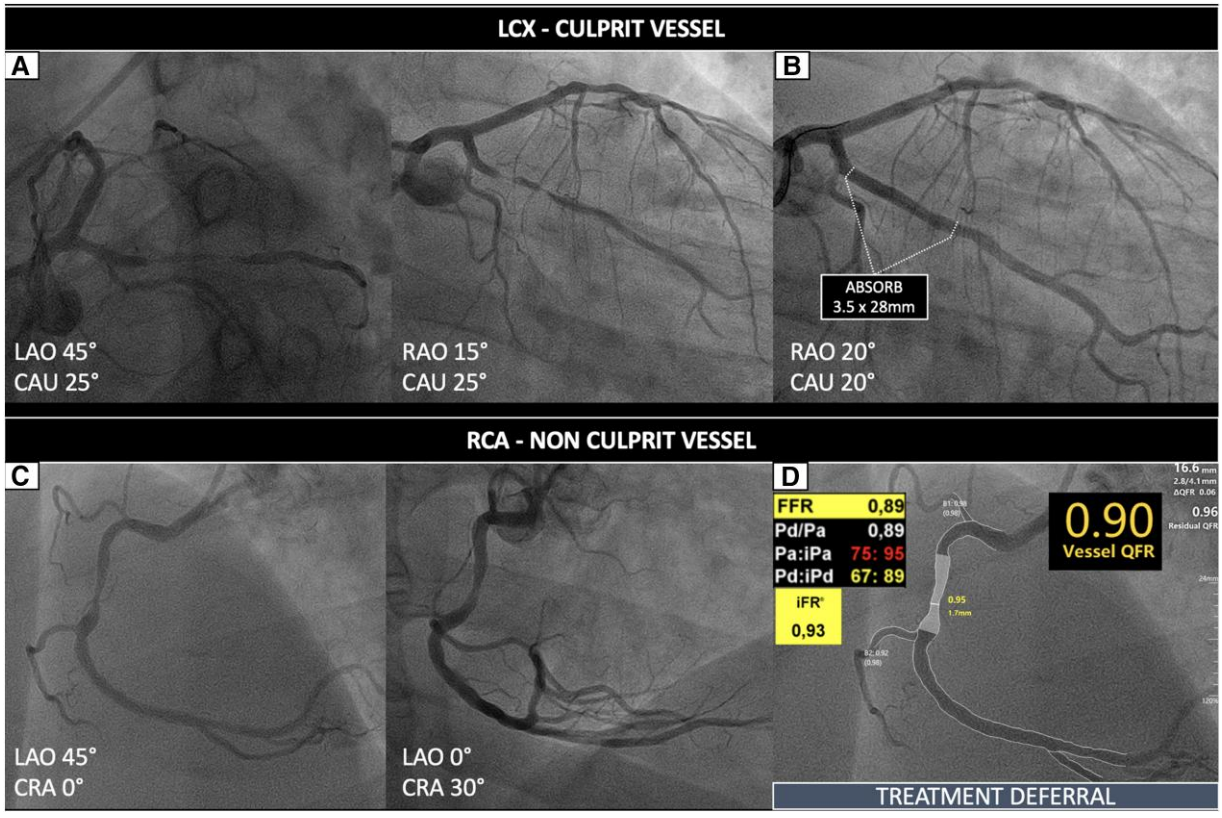

Figure 1 Invasive coronary angiography showed a sub-occlusive stenosis on a large obtuse marginal (OM) branch of the LCX (*A*), which was successfully treated with deployment of a 3.5 × 28 mm ABSORB bioresorbable vascular scaffold (*B*). A residual intermediate non-target vessel stenosis on the proximal RCA was present (*C*). After pressure wire–based physiological assessment (*D*) both at rest and under hyperaemia with detection of values well above the ischaemic threshold (iFR 0.93; FFR 0.89), deferral was decided, in keeping with current practice guidelines. CAU, caudal; CRA, cranial; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; iPa, instantaneous aortic pressure; iPd, instantaneous distal pressure; LAO, left anterior oblique; LCX, left circumflex artery; Pa, aortic pressure; Pd, distal pressure; QFR, quantitative flow ratio; RAO, right anterior oblique; and RCA, right coronary artery.

non-ischaemic findings of wire-based assessment. However, RWS analysis showed a marked hotspot in the segment of interest (maximum RWS value 27.7%), indicating the presence of vulnerable plaque. At follow-up, a severe progression of the deferred RCA was observed both from haemodynamic (μQFR 0.78) and vulnerability (RWS 34.0%) point of view.

Discussion

The occurrence of adverse events in non–flow-limiting coronary lesions could be an indication that physiological assessment alone fails to identify all high-risk coronary lesions, as recently shown in the COMBINE OCT-FFR trial.[3,5] The identification of 'true' vulnerable plaque might play a pivotal role in patients' risk stratification in patients with CAD.[6] However, the use of intravascular imaging to assess plaque vulnerability is mostly hampered by the increased costs and risks related to the invasiveness of the procedure. Therefore, further diagnostic tools to identify plaque vulnerability are urgently needed.

Historically, high wall strain patterns detected by intravascular ultrasound-derived palpography were reported as suspected to correspond to vulnerable plaque phenotypes.[7] However, the clinical utility and application of elastography/palpography has always remained extremely limited. In order to make these measurements more easily available, we have firstly developed the Superficial Wall Strain/Stress, which is based on measurements obtained in all three dimensions, after 3D coronary angiography reconstruction.[8] This technique is complex, demanding, and time-consuming, precluding its availability in the cath-lab. The recently developed RWS focuses on dimensional changes in the radial dimension and has the net advantage of being simple and easy to compute. In several '*in silico*' retrospective analyses, RWS was shown to provide additional prognostic value in the tailored patient's risk stratification in a growing number of patients (~1.500 in total). The available evidence in support of RWS use is summarized in Supplementary material online, *Table S1*.

In a validation study, maximum RWS along the coronary artery was found to positively correlate with optical coherence tomography-derived lipid burden and lipid-to-cap ratio and negatively with fibrous cap thickness.[9] Moreover, in a post-hoc analysis of the randomized FAVOR III China study investigating 824 non–flow-limiting vessels in 751 patients, maximum RWS > 12% was found to be a powerful predictor of 1 year vessel-oriented composite endpoint occurrence (adjusted hazard ratio [HR]: 4.44; 95% confidence interval [CI]: 2.43–8.14; $P < 0.001$). In this specific analysis, the residual risk after revascularization deferral based on the combination of normal RWS max and preserved μQFR was significantly reduced compared with decisions

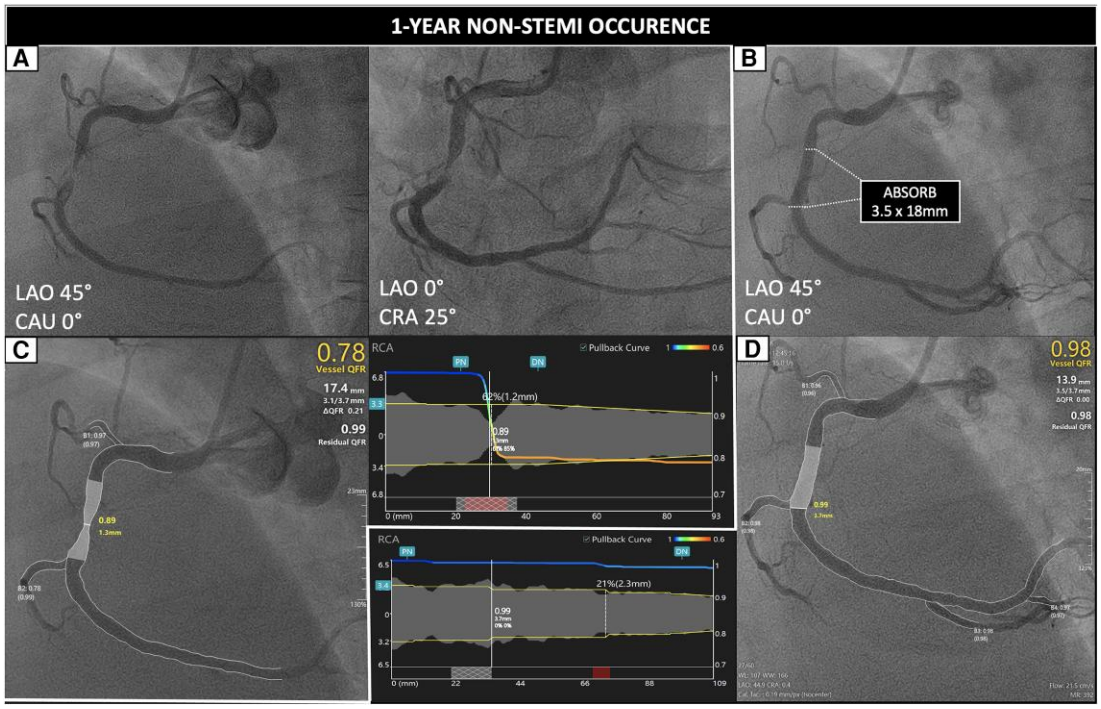

Figure 2 Invasive coronary angiography after re-admission due to an acute myocardial infarction: a severe progression of the deferred lesion on right coronary artery was present, leading to a critical stenosis with partially thrombotic occlusion (*A*). Another 3.5 × 18 mm ABSORB bioresorbable device was implanted with good final result (*B*). Angiography-derived physiology (μQFR 0.78) confirmed the severe progression of the previously untreated disease (*C*), whilst post-percutaneous coronary intervention physiology computation showed an optimal post-procedural result (*D*). STEMI, ST-elevation myocardial infarction. Other abbreviations as in *Figure 1*.

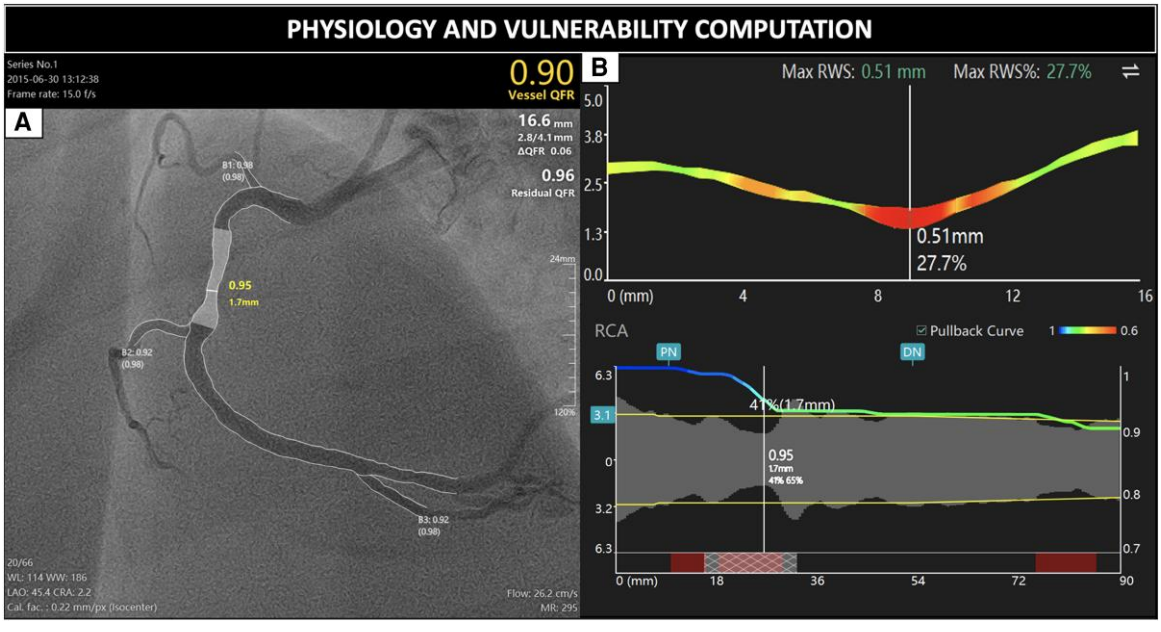

Figure 3 Baseline coronary angiogram analysis by quantitative flow ratio software (AngioPlus Core, version V3, Pulse Medical Technology Inc., Shanghai, China). Murray's law–based QFR value (μQFR 0.90) corroborated the non-ischaemic findings of pressure wire–based physiological assessment (*A*), whilst RWS computation (maximum RWS 27.7%) depicted a large hotspot in the segment of interest retrospectively identifying this plaque as vulnerable (*B*). RWS, radial wall strain. Other abbreviations as in *Figure 1*.

based on μQFR alone.[10] From a biomechanical point of view, fatigue and rupture of a fibrous cap can be caused by repetitive peaks of high radial strain, both as a result of the pulsatile rise and fall of intracoronary pressure and its interaction with vulnerable plaque.[9] Segments with high RWS associate with lipid-rich plaque that are prone to progression and plaque rupture during follow-up.[11] Therefore, the identification of RWS hotspots might potentially improve the risk stratification of non-culprit lesions and empower secondary prevention strategies.[10]

To conclude, novel imaging-based computational technologies are expected to broaden the integrated assessment of physiology and plaque vulnerability, empowering and simplifying the workflow of the decision-making process in the catheterization laboratory. High-risk patients will benefit from optimized tailored secondary prevention with emphasis on achieving strict target goals. Whether haemodynamically insignificant stenoses with high RWS should be considered for preventative stent implantation or other device-based interventions may deserve prospective testing in the future.[12]

Best of medical care by today's standards would include ezetimibe and possibly the use of PCSK-9 inhibitors. In the setting of ACS, ticagrelor or prasugrel would be preferred over clopidogrel. This patient was treated according to prevailing guidelines in 2015. Whether rapid disease progression at high-strain spots can be prevented by more efficacious contemporary secondary prevention remains to be verified.

Lead author biography

Dr Simone Fezzi is an interventional cardiology research fellow at the University of Galway, Ireland. He completed his cardiology training at the University of Verona, Italy, and his master in interventional cardiology at the University of Galway, Ireland. His main areas of interest include coronary physiology, intracoronary imaging, plaque vulnerability, and coronary intervention.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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