## Combined functional and anatomical assessment of coronary stenosis by coronary CT angiography

Daniele Andreini<sup>1,2\*</sup>, MD, PhD, FESC, FSCCT

1. Centro Cardiologico Monzino, IRCCS, Milan, Italy; 2. Department of Clinical Sciences and Community Health, Cardiovascular Section, University of Milan, Milan, Italy

During the last decade, extensive literature has confirmed the high diagnostic accuracy of coronary computed tomography angiography (CCTA) for the detection of coronary stenosis using invasive coronary angiography (ICA) as gold standard<sup>1</sup>. Based on these data and the findings of large prospective trials, such as PROMISE and SCOT-HEART, CCTA has been definitively integrated into the routine clinical management of patients with suspected coronary artery disease (CAD) as the first-line diagnostic and prognostic method<sup>2,3</sup>. The ESC Guidelines on the management of stable CAD recommend CCTA with a Class I level of evidence<sup>4</sup>. However, relying only on anatomical information with CCTA has proven to be insufficient to detect haemodynamically significant epicardial stenosis<sup>5</sup>. Recently, CT-derived fractional flow reserve (FFRCT) and stress myocardial CT perfusion (CTP) have emerged as technologies for a comprehensive evaluation of coronary stenosis, offering both anatomical (i.e., luminal and plaque) and functional assessment in one single technique. In particular, FFRCT is a well validated method for the non-invasive evaluation of coronary physiology with high agreement with invasive FFR6. Growing evidence supports ICA deferral when FFRCT is negative and a higher PCI/ICA ratio when decisions around ICA are FFRCT-guided7. However, the commercially available option for FFRCT computation still requires image data transfer to external supercomputers and remains time-consuming, whereas, for more rapid FFRCT derivation, simplified on-site workstation-based prototype algorithms have been developed with promising results8. In this issue of EuroIntervention, Westra et al report a prospective multicentre

study aimed at assessing the diagnostic performance of a novel CCTA-based method for on-site calculation of FFR (CT-QFR) in 278 symptomatic patients<sup>9</sup>.

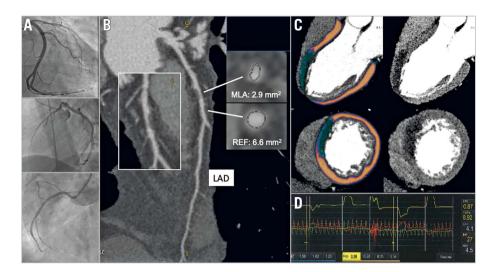
## Article, see page 576

The diagnostic performance of CT-QFR was compared with myocardial perfusion scintigraphy (MPS) and cardiovascular magnetic resonance (CMR) as second-line tests (randomised 1:1) in patients presenting with obstructive CAD on CCTA, by using invasive FFR as standard of reference. Patient-level diagnostic accuracy was better for CT-QFR than for both MPS (82.2% vs 70.3%, p=0.029) and CMR (77.0% vs 65.5%, p=0.047). Following a positive CCTA and with the intention to diagnose, CT-QFR, CMR and MPS were equally suitable as rule-in and rule-out modalities, with better sensitivity of CT-QFR. A strength of the study which is worthy of mention is that the authors compared the CT-QFR results with those of two largely validated stress tests, namely CMR and MPS, both recommended in the Guidelines (level of evidence 1)<sup>4</sup>, demonstrating CT-QFR to be a promising tool to detect flow-limiting stenosis. As a potential weakness of the method, the rate of unfeasible CT-QFR was not negligible (17% of CCTAs). Regarding the alternative functional CT-based method, stress CTP requires an additional scan, use of a stressor agent and is associated with higher radiation exposure but, on the other hand, may provide information on both macrovascular and microvascular disease status<sup>10</sup> (Figure 1). In summary, functional assessment with CTP or FFRCT can improve decision making in patients with CAD detected at CCTA.

\*Corresponding author: Centro Cardiologico Monzino, Via Carlo Parea 4, 20138 Milan, Italy. E-mail: daniele.andreini@ccfm.it

© Europa Digital & Publishing 2021. All rights reserved.

DOI: 10.4244/EIJV17I7A96



**Figure 1.** Myocardial ischaemia detected by stress CT perfusion. A 54-year-old man, previous PCI and DES in the mid-distal portion of a dominant left circumflex artery, symptomatic for exertional angina. ICA was negative for in-stent restenosis or de novo stenosis (A). CCTA showed an intermediate stenosis (50-55%) in the middle portion of the left anterior descending artery (LAD), with a minimal lumen area of 2.9 mm<sup>2</sup> at cross-sectional reconstruction (B). Stress CTP long- and short-axis reconstructions (C) showed a transmural perfusion defect of the anterior interventricular septum. Invasive physiological assessment (D) demonstrated microvascular dysfunction in the territory of the LAD without functional relevance of the epicardial stenosis (IMR=27, FFR=0.87).

## **Conflict of interest statement**

The author has no conflicts of interest to declare.

## References

1. Knuuti J, Ballo H, Juarez-Orozco LE, Saraste A, Kolh P, Saskia Rutjes AW, Jüni P, Windecker S, Bax JJ, Wijns W. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. *Eur Heart J.* 2018;39:3322-30.

2. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, Cole J, Dolor RJ, Fordyce CB, Huang M, Khan MA, Kosinski AS, Krucoff MW, Malhotra V, Picard MH, Udelson JE, Velazquez EJ, Yow E, Cooper LS, Lee KL; PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med.* 2015;372:1291-300.

3. SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. *Lancet.* 2015;385:2383-91.

4. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Valgimigli M, Achenbach S, Bax JJ; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2020;41:407-77.

5. Meijboom WB, Van Mieghem CA, van Pelt N, Weustink A, Pugliese F, Mollet NR, Boersma E, Regar E, van Geuns RJ, de Jaegere PJ, Serruys PW, Krestin GP, de Feyter PJ. Comprehensive assessment of coronary artery stenoses: computed tomography coronary angiography versus conventional coronary angiography and correlation with fractional flow reserve in patients with stable angina. *J Am Coll Cardiol.* 2008;52:636-43. 6. Driessen RS, Danad I, Stuijfzand WJ, Raijmakers PG, Schumacher SP, van Diemen PA, Leipsic JA, Knuuti J, Underwood SR, van de Ven PM, van Rossum AC, Taylor CA, Knaapen P. Comparison of Coronary Computed Tomography Angiography, Fractional Flow Reserve, and Perfusion Imaging for Ischemia Diagnosis. *J Am Coll Cardiol.* 2019;73:161-73.

7. Fairbairn TA, Nieman K, Akasaka T, Nørgaard BL, Berman DS, Raff G, Hurwitz-Koweek LM, Pontone G, Kawasaki T, Sand NP, Jensen JM, Amano T, Poon M, Øvrehus K, Sonck J, Rabbat M, Mullen S, De Bruyne B, Rogers C, Matsuo H, Bax JJ, Leipsic J, Patel MR. Real-world clinical utility and impact on clinical decision-making of coronary computed tomography angiography-derived fractional flow reserve: lessons from the ADVANCE Registry. *Eur Heart J.* 2018;39:3701-11.

8. Coenen A, Kim YH, Kruk M, Tesche C, De Geer J, Kurata A, Lubbers ML, Daemen J, Itu L, Rapaka S, Sharma P, Schwemmer C, Persson A, Schoepf UJ, Kepka C, Yang DH, Nieman K. Diagnostic Accuracy of a Machine-Learning Approach to Coronary Computed Tomographic Angiography-Based Fractional Flow Reserve: Result From the MACHINE Consortium. *Circ Cardiovasc Imaging*. 2018;11:e007217.

9. Westra J, Li Z, Rasmussen LD, Winther S, Li G, Nissen L, Petersen SE, Ejlersen JA, Isaksen C, Gormsen LC, Urbonaviciene G, Eftekhari A, Weng T, Qu X, Bøtker HE, Christiansen EH, Holm NR, Bøttcher M, Tu S. One-step anatomic and function testing by cardiac CT versus second-line functional testing in symptomatic patients with coronary artery stenosis: head-to-head comparison of CT-derived fractional flow reserve and myocardial perfusion imaging. *EuroIntervention.* 2021;17:576-83.

10. Andreini D, Mushtaq S, Pontone G, Conte E, Collet C, Sonck J, D'Errico A, Di Odoardo L, Guglielmo M, Baggiano A, Trabattoni D, Ravagnani P, Montorsi P, Teruzzi G, Olivares P, Fabbiocchi F, De Martini S, Calligaris G, Annoni A, Mancini ME, Formenti A, Magatelli M, Consiglio E, Muscogiuri G, Lombardi F, Fiorentini C, Bartorelli AL, Pepi M. CT Perfusion Versus Coronary CT Angiography in Patients With Suspected In-Stent Restenosis or CAD Progression. *JACC Cardiovasc Imaging.* 2020;13:732-42.