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EDITORIAL

How will coronary physiology, plaque vulnerability and ischemia be integrated in future patient pathways with chest pain?

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1. Introduction

The rapid development of noninvasive imaging in cardiology has facilitated a paradigm shift in the diagnosis of coronary artery disease over the last 20 years. For several decades, invasive coronary angiography was the gold standard, default test for diagnosing coronary artery disease but with rapid technological improvements in the quality of computed tomography coronary angiography (CTCA), this test has become dominant in many centers. CTCA allows for the identification not only of the presence and extent of coronary atheroma, but can also provide increasingly sophisticated data regarding plaque composition, including markers of risk. Moreover, using fluid dynamics computer modeling, noninvasive assessment of fractional flow reserve can be derived from CTCA datasets when coupled with some basic clinical parameters. These advances continue to stimulate changes to the clinical pathway of patients presenting with chest pain of recent onset.

2. Review of current chest pain pathways in the UK

In 2016, the use of CTCA was recommended as the default test for the majority of stable patients by the NICE CG95 Guidelines for Chest Pain of Recent Onset [1]. This recommendation was driven by data including particularly the 5 year follow-up of SCOT-HEART study, which demonstrated prognostic benefit for a CTCA upfront strategy in 4146 patient with stable chest pain when compared to routine care [2]. Specifically, at a median follow-up 4.8 years, patients who underwent a CTCA strategy had a significantly lower incidence of a combination of death from coronary heart disease or non-fatal myocardial infarction, compared with routine assessment (2.3% CT group vs 3.9% standard care). This difference was driven by the rate of MI, but not death. It is notable that, perhaps counter-intuitively, the rates of coronary angiography/revascularisation were similar at 5 years (491 CT group vs 502 standard care). It has been hypothesized that the clinical benefit derives from the application of disease-modifying medical therapy in the CTCA group, having had coronary atheroma identified early in the care pathway. Other trials, including PROMISE have also shown equivalence for an up-front CTCA strategy in stable chest pain patients compared to routine functional testing [3].

By contrast, the clinical value of routine early CTCA in patients with acute coronary syndrome has not been established. The RAPID CTCA trial tested the early use of CTCA versus standard care on the 1-year clinical outcomes in 1749 patients presenting with a provisional diagnosis of non-ST elevation MI and one or more of: 1) previous coronary heart disease; 2) elevated troponin; 3) abnormal ECG. The primary outcome was all cause death or myocardial infarction at 1 year [4]. There was no difference in the primary outcome between the groups (5.8% CT group vs 6.1% standard of care, $p = 0.65$), and, although CTCA was associated with a reduced rate of invasive angiography, this arm also had longer length of stay.

3. FFR_{CT}

FFRCT uses the dataset from CTCA to model flow limitation and derive FFR, validated against invasive angiography and pressure wire-derived FFR [5]. In a series of observational studies, including PLATFORM [6] and ADVANCE [7], and now 2 randomized trials (FORECAST [8] & PRECISE [9]), the clinical utility of FFR_{CT} in stable patients compared to routine care can be summarized as follows: (i) quicker care pathway to management plan; (ii) significantly fewer patients having invasive coronary angiography (ICA); (iii) significantly less ICA showing no obstructive coronary disease; (iv) no difference in MACE rate; (v) cost neutral in the NHS.

Additionally, the recent FISH & CHIPS UK Registry recently reported a lower CV mortality after adoption of FFR_{CT} across Trusts in the NHS [10]. Finally, the FFRCT analysis, thanks to deep learning artificial intelligence platforms, can now offer sophisticated automated assessment of adverse plaque and hemodynamic characteristics that predict the risk of individual plaque lesions causing acute coronary syndrome (ACS) events in the future: the potential clinical utility of which is substantial.

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4. CTCA: assessment of plaque risk, perivascular inflammation & prognosis

There is rapidly accumulating evidence that some features of plaque composition as defined on CTCA are associated with risk of future substrate for ACS, including plaque volume, low attenuation plaque, napkin-ring sign, spotty calcification and positive remodeling [11]. For example, a sub study analysis from the RAPID-CTCA trial has demonstrated that low attenuation plaque burden is predictive of 1 year mortality or recurrent myocardial infarction, independent of GRACE score and obstructive coronary artery disease [12]. In addition, CTCA plaque characterization can discriminate between type 1 and type 2 myocardial infarction [13]. Such findings have been reproduced in multiple independent studies, as reviewed in references [14,15]. Furthermore, in the EMERALD study, the use of a combination of adverse plaque characteristics and adverse hemodynamic characteristics using FFR_{CT} yielded a stepwise, dose-dependent risk stratification for lesion-specific risk of subsequent ACS [8].

CTCA data has also been used to derive and validate the Fat Attenuation Index (FAI), a quantification of the dynamic status of coronary perivascular fat metabolism that is a surrogate for local inflammation [11]. Using this novel tool, it has been shown that FAI, tested on 2 distinct patient populations, is associated with medium term mortality in the CRISP CT study [16].

These data have recently been augmented by the deployment of deep learning artificial intelligence to amplify the ability to incorporate multiple inter-related factors in complex models for prediction of lesion risk, and consequent patient prognosis. Examples are available in EMERALD2 [17] and the ORFAN EAT study [18]. Further clinical validation of these AI-based concepts is likely to yield powerful new tools with which to risk stratify patients, particularly in the field of primary prevention, using much more precise algorithms than we currently employ pathways that will incorporate a hierarchy of conventional clinical factors as well as CTCA-based and novel blood biomarkers in turn. This will inevitably open avenues for investigation into prophylactic interventions to prevent high risk plaques from following their natural trajectory. As with all CT based imaging there is a radiation risk to the patient involved, and therefore we would generally not recommend interval CT scanning unless the patient develops new symptoms consistent with myocardial ischemia. As demonstrated in SCOT-HEART, early targeted interventions to lower modifiable cardiovascular risk factors is the clear goal of advanced CT imaging of the coronary vasculature.

5. Conclusion

Evidence already justifies the application of CTCA as a default investigation in patients with stable chest pain. The facility to combine anatomical and physiological vessel assessment using FFR_{CT} already offers a safe and efficient novel pathway for such patients. A rapidly growing body of data using AI-dependent complex models that incorporate variables of patient-specific, vessel-specific, and plaque-specific features are leading us to a new era of promise for tailored primary prevention medicine for subclinical coronary artery disease.

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References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. Nice Clinical Guideline. 2010.
2. Newby DE, Adamson PD, Berry C, et al. Coronary CT angiography and 5-year risk of myocardial infarction. N Engl J Med. 2018 Sep;379(10):924–933.
•• **Landmark paper describing the utilization of CTCA for patients with stable angina.**
3. Hoffmann U, Ferencik M, Udelson JE, et al. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the PROMISE trial (prospective multicenter imaging study for evaluation of chest pain). Circulation. 2017 Jun;135(24):2320–2332.
4. Gray AJ, Roobottom C, Smith JE, et al. Early computed tomography coronary angiography in patients with suspected acute coronary syndrome: randomised controlled trial. BMJ. 2021 Sep;374:n2106. doi: 10.1136/bmj.n2106
5. Hecht HS, Narula J, Fearon WF. Fractional flow reserve and coronary computed tomographic angiography: a review and critical analysis. Circ Res. 2016 Jul;119(2):300–316. doi: 10.1161/CIRCRESAHA.116.307914
6. Douglas PS, Pontone G, Hlatky MA, et al. Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFR(CT): outcome and resource impacts. Eur Heart J. 2015 Dec;36(47):3359–3367.
7. Patel MR, Nørgaard BL, Fairbairn TA, et al. 1-year impact on medical practice and clinical outcomes of FFR(CT): the ADVANCE registry. JACC: Cardiovasc Imaging. 2020 Jan;13(1):97–105.
8. Curzen N, Nicholas Z, Stuart B, et al. Fractional flow reserve derived from computed tomography coronary angiography in the assessment and management of stable chest pain: the FORECAST randomized trial. Eur Heart J. 2021 Oct;42(37):3844–3852. doi: 10.1093/eurheartj/ehab444
• **Important trial regarding FFRct and cost effectiveness and clinical outcomes in patients with stable chest pain.**
9. Douglas PS, Nanna MG, Kelsey MD, et al. Comparison of an initial risk-based testing strategy vs usual testing in stable symptomatic

patients with suspected coronary artery disease: the PRECISE randomized clinical trial. JAMA Cardiol. 2023 Oct;8(10):904–914.
10. Fairbairn F. CT FFR in stable heart disease and coronary computed tomographic angiography helps improve patient care and societal costs. Eur Heart J. 2023;44(Supplement_2):ehad655.161. doi:10.1093/eurheartj/ehad655.161
11. Lee JM, Choi G, Koo BK, et al. Identification of high-risk plaques destined to cause acute coronary syndrome using coronary computed tomographic angiography and computational fluid dynamics. JACC Cardiovasc Imaging. 2019 Jun;12(6):1032–1043.
12. Meah MN, Tzolos E, Wang KL, et al. Plaque burden and 1-year outcomes in acute chest pain: results from the multicenter RAPID-CTCA trial. JACC Cardiovasc Imaging. 2022 Nov;15 (11):1916–1925.
13. Meah MN, Bularga A, Tzolos E, et al. Distinguishing type 1 from type 2 myocardial infarction by using CT coronary angiography. Radiol Cardiothorac Imaging. 2022 Oct;4(5):e220081.
14. Kwiecinski J, Tzolos E, Williams MC, et al. Noninvasive coronary atherosclerotic plaque imaging. JACC Cardiovasc Imaging. 2023 Dec;16(12):1608–1622.
15. Emfietzoglou M, Mavrogiannis MC, Samaras A, et al. The role of cardiac computed tomography in predicting adverse coronary events. Front Cardiovasc Med. 2022;9:920119. doi: 10.3389/fcvm.2022.920119
16. 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 (London, England). 2018 Sep;392(10151):929–939. doi: 10.1016/S0140-6736(18)31114-0
- **Important study linking coronary inflammation to cardiovascular risk.**
17. Koo B-K. Artificial intelligence-enabled quantitative plaque and hemodynamic analysis for predicting acute coronary syndrome risk and prevention strategy: the EMERALD II Study. TCT Conf. USA, 2023.
18. West HW, Siddique M, Williams MC, et al. Deep-learning for epicardial adipose tissue assessment with computed tomography: implications for cardiovascular risk prediction. JACC Cardiovasc Imaging. 2023;16(6):800–816. doi: 10.1016/j.jcmg.2022.11.018