ORIGINAL ARTICLE

CT CORONARY ANGIOGRAM WITH FFR CT – A REVOLUTION IN THE DIAGNOSTIC FLOW OF CORONARY ARTERY DISEASE

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Background: Within the last few years, advances in CT coronary imaging has revolutionised the diagnostic flow of suspected coronary artery disease. CT coronary angiogram has a high diagnostic accuracy and negative predictive value for diagnosis of coronary disease. Its non-invasive nature makes it a lower risk and lower cost procedure compared to conventional invasive coronary angiogram. However, there is restricted value in anatomical evaluation without input regarding the functional significance of each lesion identified with cross-sectional imaging. The gold standard to assess whether a lesion is haemodynamically significant has been the assessment of FFR (fractional flow reserve). Fractional flow reserve is the ratio between maximum coronary flow in the presence of stenosis and in the hypothetical absence of stenosis. This is measured invasively by introducing a pressure wire across the lesion involving intracoronary nitro-glycerine as well as intravenous infusion of adenosine. However, the introduction of FFR CT provides information on functional significance of a lesion only using the CT data set of CT CA. Through complex non-linear equations and supercomputing, it produces a three-dimensional model of the coronary artery giving FFR values at multiple point along every major coronary vessel. It is non-invasive, involves no extra dose or contrast and does not require adenosine stress. A lesion that may appear moderate to severe on CT CA with FFR values above 0.80 can be managed by optimal medical management alone. Together FFR Ct and CTCA provide a comprehensive assessment for CAD leading to a reduction in downstream testing and unnecessary revascularisation procedures.

Keywords: Coronary artery disease; CT CA; FFR CT

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INTRODUCTION

The latest advances in CT imaging over the last ten years or so have resulted in a paradigm shift in the assessment of coronary artery disease.[1] Two radiologists wrote this review with years of clinical experience with CT CA and proficiency in FFR CT assessment. It reviews the technique, indications, clinical use and limitations of FFR CT in coronary artery disease. We will also review clinical trials and shed light on future directions in which FFR CT will expand its use in the coming years.

Better imaging acquisition, as well as post processing techniques with CTCA, have resulted in greater anatomical detail of coronary artery plaques. CTCA now not only enables more accurate assessment of the degree of luminal stenosis, but also provides additional risk stratification information, by providing detailed information on high-risk plaque features such as House field values, positive vessel remodelling at the site of plaque and the napkin ring sign.[2–4] Plaque burden[5] and the ratio of coronary vessel volume to myocardial mass[6] can provide further risk stratification.

National institute of clinical excellence guidelines have also updated the guidelines for chest pain and now recommend CTCA as the initial diagnostic test for patients with stable chest pain and suspected coronary artery disease.[7]

However, the degree of luminal stenosis does not provide quantitative information on the functional significance of that lesion under stress conditions, particularly for moderately (50–70%) stenotic lesions. Using the visual assessment of vessel stenosis alone without the findings being supported by quantitative coronary angiographic techniques frequently results in revascularisation undertaken for lesions that are not haemodynamically stable or not the culprit of the patient's symptoms.[8]

This haemodynamic / function significance is of paramount importance in the management of a culprit lesion and to avoid unnecessary intervention. Thus far, the most commonly used technique to get that information had been to perform an invasive FFR test in the catheterisation lab. FFR involves catheterisation of the coronary tree with pressure wires passed through all suspected lesions and values are recorded within the area of stenosis and beyond it. This also requires an intravenous infusion of adenosine as well as intracoronary nitro-glycerine injection during the procedure.[9]

Functional flow reserve (FFR) is the ratio between maximum coronary flow in the presence of stenosis and the maximum coronary flow in the hypothetical absence of stenosis. Practically it is calculated as the ratio of pressure between the distal parts of atheromatic plaque divided by the pressure in the proximal part of the vessel during maximal hyperaemia, achieved by continuous infusion of adenosine. Several clinical trials that have demonstrated the accuracy and reliability of FFR values to guide the decision to revascularisation, including the FAMI I, FAME II and DEFER Trials.[10–12] However given the risk involved with the invasive nature of the test and also taking account risk and cost of adenosine and iodinated contrast medium and Cath lab time, despite its usefulness it is infrequently used in clinical practice.[13,14] Of the recent advances in cross-sectional coronary imaging, the most revolutionary has been that of FFR CT. It aims to provide information on the functional significance similar to invasive FFR but does so not only for a culprit lesion but also for the whole coronary tree using only the data set of the CT coronary angiogram. The Navier-Stokes equations form the basis of the computational flow dynamics behind FFR CT assessment.[15] Coronary velocity and flow in every segment of the coronary vascular tree is calculated with the use of supercomputing and complex non-linear equations continuous calculations of pressure reproduced through milliseconds of the entire cardiac cycle.

As a result, a three-dimensional model of the coronary arteries is produced specifically for every patient. This model is based on three scientific principles: 1). The resting coronary blood flow can be quantified relative to myocardial mass. This mass can be calculated from the myocardial volume, extracted from the volumetric CTCA data. 2) Microcirculatory resistance at rest is inversely proportional to the size of the lumen. 3) Vasodilatory response to adenosine is predictable.[16] The model represents the combination of anatomical and functional characteristics of each patient based. Of note is that the FFR values are highly reproducible. According to a study, the difference between first and second FFR CT analyses was 0.035 and for invasive FFR repeat measurements was 0.043.[17]

A threshold value of 0.8 is used in both invasive and CT FFR. A post stenotic FFR CT value less than or equal to 0.80 indicates the possibility of haemodynamic significance.[18,19] Alternatively, an FFR CT value greater than 0.80 indicates that a lesion is unlikely to be haemodynamically significant. It can, therefore, be managed with optimal medical treatment eliminating the need for further downstream testing.[20,21]

Values <0.75 are indicative of significant functional ischemia. There is also the highest agreement between invasive FFR and FFRCT values at or below 0.75.[20] There is a slightly ambiguous zone between 0.75–0.80 and clinical management for lesions with values lying between 0.75–0.80 would require further correlation with other risk factors and CT imaging factors. Further decision will depend in such cases on not only the specific vessel involved, location of stenosis and plaque burden but also on patient individual cardiovascular stratification. It is recommended that for smaller and side branch lesion, even for FFR CT values of or lower than 0.75 patients can be managed with optimal medical management instead of referral to invasive angiography.[22]

FFRCT values are given for the entire length of the two main systems and major branches, unlike invasive FFR that only gives information on the specific lesion through which the wire is advanced. The 3-dimensional model gives specific values at various points along every interpretable vessel. However, it is recommended that FFR values 2–3 cm distal to the lesion be used for interpretation of haemodynamic compromise caused by that lesion and not the value at maximum luminal narrowing itself.[23] This is to avoid the effect of pressure recovery phenomenon on FFR values pertaining to that lesion. FFR values may progressively decrease downstream to a lesion. This may be due to diffuse coronary artery disease or the effect of serial lesion. In the case of serial lesions, to determine which lesion is contributing to the flow limiting nature of disease would be hard to ascertain.

It is recommended in case of serial lesions, FFR value 10–20 mm from each lesion be reported to assess haemodynamic significance. The vessels with progressive FFR values drop without an identifiable culprit lesion warrant further risk stratification and investigation. It is crucial to keep in mind that FFR values should not be used alone when determining the need for ICA or revascularisation.[24]

Smaller or side branch vessels that may be overlooked at the time of assessment with CTCA may reveal values of <0.80 with FFR. Although these they may not be significant, they may contribute to FFR values within the parent vessel. Lesions which appear to cross severe stenosis on CTCA and have FFR CT values above 0.80 can be safely managed medically without revascularisation, follow up of such patients reveals no adverse event, as demonstrated by the invasive arm of the platform trail for patients that were deferred from invasive angiography based on FFR CT results.[25]

As with any diagnostic modality, there are some limitations to the assessment of CTCA cases with FFR CT of which inability to process cases with stents & by-pass grafts is perhaps the most significant one. FFRCT cannot be evaluated in patients with by-pass grafts altogether. IN case of coronary stents, the vessel with astet in situ cannot be analysed and is shaded as grey in the coronary functional analysis. However, if the stents are in the left main stem stent or both main vessels (e.g. LAD & RCA) cases are not processed altogether.

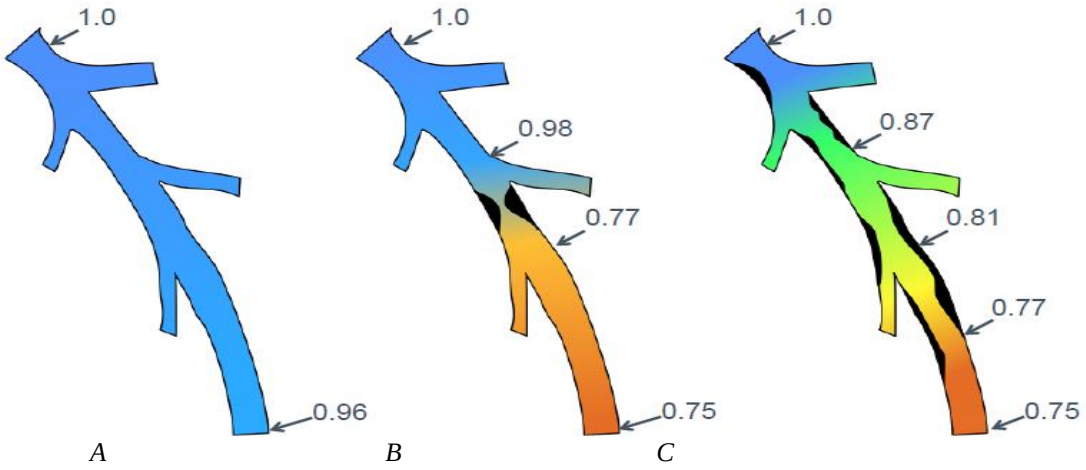

Figure-1: A Normal: No significant drop in FFR value
B Focal significant stenosis with immediate drop in FFR (culprit lesion-target for PCI)
C Diffuse multifocal disease with moderate stenosis causing gradual drop in FFR values. (No identifiable PCI target)

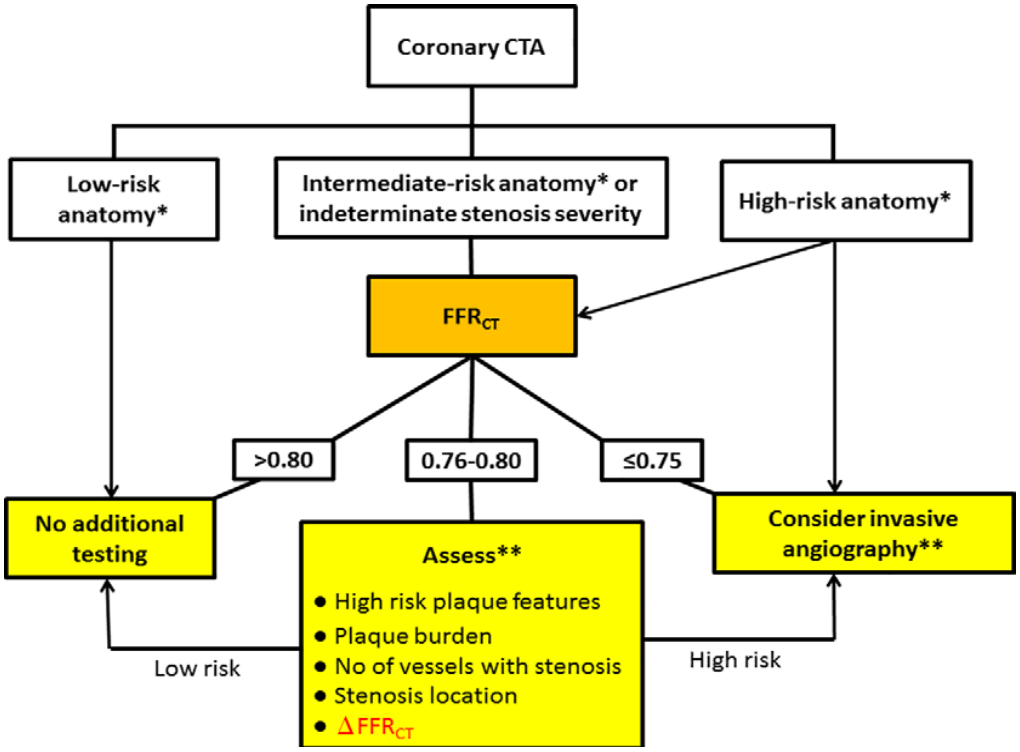

Figure-2[26]: FFRCT appropriateness and interpretation recommendation. * = Low risk: patients either Without coronary disease or with maximum stenosis less than 30%. Intermediate risk: patients with one or more intermediate range stenosis (30%–69%). High risk: patients with left main, three-vessel disease or stenosis 70% or greater. (CTA). ** = Post-test risk stratification: Test results must always be evaluated in their clinical context, patient preferences as well as high-risk anatomic features and likelihood of revascularisation[26]

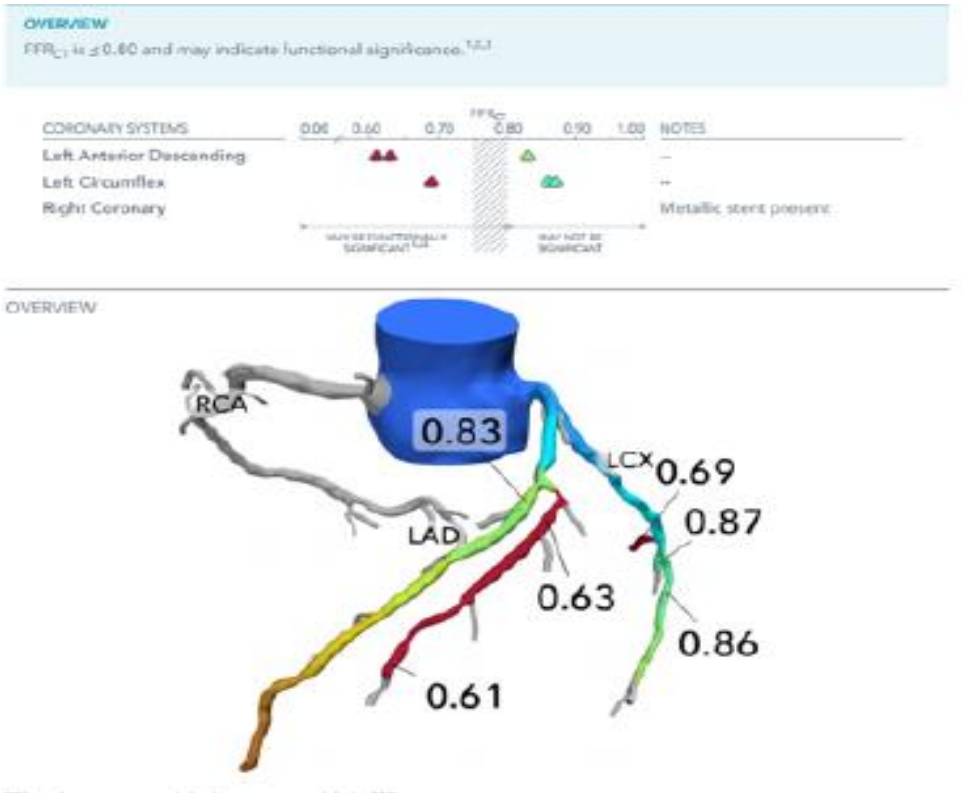

Figure-3: RCA with stent greyed out in analysis.

FFR CT calculates maximum hyperaemia resulting from vasodilation of coronary tree therefore sublingual nitrate administration with a dose of 0.8 mg, 3–5 min before acquisition is essential for evaluation. In patients with contraindication to nitrate use, this does affect the results of FFR evaluation.

Similar to all cross-sectional techniques, image quality is of utmost importance for an accurate assessment. Multiple areas of anatomically ill-defined margins of the vascular lumen, resulting from movement, malalignment or inadequate heart rate control may lead to an inability to process. Adjustments in reconstructed data set to achieve better contrast-to-noise ratio is recommended in all cases.

High calcium score, although previously thought to limit FFR CT assessment is, in our opinion, not a significant factor contributing to the inability of the software to process the data set. In our experience, FFR CT has been able to successfully process cases with coronary artery calcium scores close to 4000.

Various research studies have demonstrated FFRCT for safety, accuracy and cost-effectiveness. FFRCT RIPCORD study demonstrated that FFRCT results had a significant effect on the determination of significant CAD and management of patients compared to coronary CTA alone.[27] PLATFORM (Prospective Longitudinal Trial of FFRCT: Outcome and Resource Impacts) prospective multicentre trial has positively demonstrated the utility of FFR CT to assess clinical outcomes.[28] The NXT (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) in which patients underwent coronary CTA and FFRCT before the planned ICA. It reported that the per-vessel sensitivities and specificities were 84% and 86% respectively.[18]

Syntax score (Synergy between PCI with Taxus and Cardiac Surgery) scores are traditionally assessed invasively and help the clinical team decide the best course of action for the patient. Recently calculation of the non-invasive functional SYNTAX score utilizing FFRCT has yielded similar results to those obtained invasively and reclassified 30% of patients from the high- and intermediate-SYNTAX score to the low-risk.[29]

More recent advances such as those of virtual stenting using FFR has shown incredible promise in order to demonstrate the likelihood of ischemia caused by a lesion when placed under stress conditions with diagnostic accuracy close of 96%.[30]

CONCLUSION

FFR CT is a revolutionary technique in the non-invasive evaluation of coronary artery disease. The updated UK NHS NICE CG95 guidance recommends CTCA as the first-line investigation for evaluation of new-onset of typical/atypical chest pain and recommends functional imaging with FFR CT for lesions causing moderate stenosis identified on CTCA[2]. However, FFR values should always be correlated with CT coronary angiogram findings. The patient's clinical information and risk stratification are also equally important in the flow of further downstream testing and decision of revascularisation for the specific lesion. It can act as a gatekeeper to Cath lab time, transforming pathways and potentially eliminating revascularisation procedures being undertaken for non-haemodynamically significant lesions. CTCA with FFR CT in the assessment of flow-limiting coronary disease decreases the overall time from diagnosis to treatment, potentially establishing a one-stop-shop test. FFR CT is a relatively new and evolving technique, and the future will see a broadening of its clinical utilization.

AUTHORS'S CONTRIBUTION

ME: Literature search, proof reading, write-up. SR: Write-up, literature search, proof reading. Both authors contributed equally

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