

CT FFR A paradigm shift in evaluation of coronary artery disease

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Invasive catheter coronary angiography has long been considered the reference standard for diagnosis of coronary artery disease. Decisions regarding revascularization procedures have traditionally been based on visual assessment of severity of coronary artery disease, often termed occluso-stenotic reflex. 70% is the cutoff to decide on revascularization. However, there are numerous limitations of visual interpretation, significant inter and intra observer variability as well as factors other than luminal diameter narrowing, that influence the physiologic significance of a focal narrowing. Whether the narrowing is focal or diffuse, single or multiple, lesion length, shape and eccentricity as well as presence of collaterals. The decision to revascularize coronary artery stenosis should be governed by hemodynamic significance of a lesion rather than visual angiographic severity.

Fractional flow reserve (FFR) is an invasive technique performed at the time of cardiac catheterization to determine the maximal achievable blood flow in the presence of a stenosis versus maximal flow in the absence of stenosis. Essentially to determine how much blood flow at maximal hyperemia is being reduced by the lesion thus determining the hemodynamic significance of the lesion. To determine FFR, pressure at the aortic level as well as distal to the lesion at maximal hyperemia is taken during cardiac catheterization. This ratio provides the FFR value. A value below 0.8 is considered to be hemodynamically significant.

The FAME^[1] trial looked at two groups – one group received percutaneous coronary intervention solely on the basis of visual stenosis on angiography, and the second received percutaneous coronary intervention based on a FFR below 0.8. The primary end point for the study was death, myocardial infarction and repeat revascularization. The purpose of any therapy is to reduce the incidence of all these three end points. In the FAME trial, there was a 72% reduction in the primary endpoint in the second group (FFR group). The long-term efficacy of this study was confirmed in 2 and 5 year follow-ups. This has led to a paradigm shift towards using functional/hemodynamic significance of a coronary lesion (FFR) rather than anatomic severity of coronary stenosis. In current practice based on visual assessment, all stenosis above 70% are revascularized. An interesting observation of the FAME trial was 20%

of lesions above 70% had a FFR above 0.8 thus received intervention with no benefit. The reason being FFR takes into account ante grade as well as collateral flow, but visual assessment takes into account only ante grade flow. Chronically infarcted myocardium may have a visually significant stenosis. Vascularizing this will be of no value. Chronically infarcted myocardium has a low metabolic requirement. Therefore, the flow will not be reduced and FFR will not be reduced. In the FAME study, more importantly 35% of lesions with a visual assessment between 50-70% had a FFR below 0.8 and would benefit from intervention. This is as long/tandem or proximal lesions may cause compromise in supply to large parts of myocardium, though the stenosis may not be angiographically significant, the FFR will be low. Therefore, FFR is of paramount importance to decide on revascularization especially for stenosis between 50-80%.

CT coronary Angio over the last decade has evolved into a premier tool for noninvasive evaluation of coronary arteries. It has excellent negative predictive value. Thus, its ability to rule out coronary artery disease is excellent. Its positive predictable value is moderate as it tends to overestimate stenosis, nearly 50% of significant lesions on CT do not have flow limiting disease on invasive FFR. Further, it provides only anatomic information and no functional information. To obtain functional information noninvasive myocardial perfusion studies need to be performed. All these studies stress the heart. Single photon emission CT (SPECT), CT perfusion, MR perfusion studies may be performed. SPECT is the most popular comprising of more than 90% of all noninvasive myocardial perfusion test performed. It has its share of limitations, there is a significant radiation burden due to the radiopharmaceutical used. Another significant limitation is its diagnostic capabilities are based on relative distribution of radiopharmaceuticals in the myocardium. This is qualitative/subjective evaluation. If there is a balanced distribution between the coronary artery territories as happens in triple vessel disease the study will be falsely negative. Other noninvasive tests such as CT perfusion and MR perfusion have a slightly higher accuracy than SPECT, but are unfortunately not widely used due to their limited availability, limited expertise and cost.

The ideal would be to have a single study providing anatomical and functional information in a single

noninvasive test. Since CT Angio fulfils the anatomic requirements, it is only logical to utilize its capabilities further.

CT FFR has been developed which applies. Computational fluid dynamic techniques to the CT Angio data. This estimates FFR values throughout the coronary artery tree. Since virtual hyperemia is built into the model there is no need to stress the heart or use adenosine. This is ideal as in one test without stressing the heart. Numerous studies such as DISCOVER- FLOW,^[2] Follow up-NXT^[3] have compared the efficacy of CT FFR to invasive FFR with excellent correlation. In fact, CT FFR reclassified 68% of false positives on CTA as true negatives thus sorting out the limitation of CTA of moderate predictive value. There was a reduction of 61% catheter angiograms in patients with >50% stenosis based on CTFRR.

Another significant limitation of CT Angio are calcific plaques. These tend to bloom on CT Angio thus obscuring

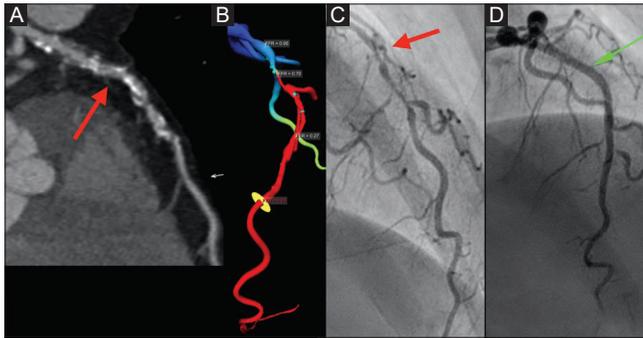


Figure 1 (A-D): (A) CT Angio demonstrates diffuse disease with soft and calcific plaques in proximal LAD. (B) CT FFR demonstrates low FFR 0.70 (red). (C) Invasive catheter angio confirms marked narrowing (D) Post angioplasty angiogram shows excellent result

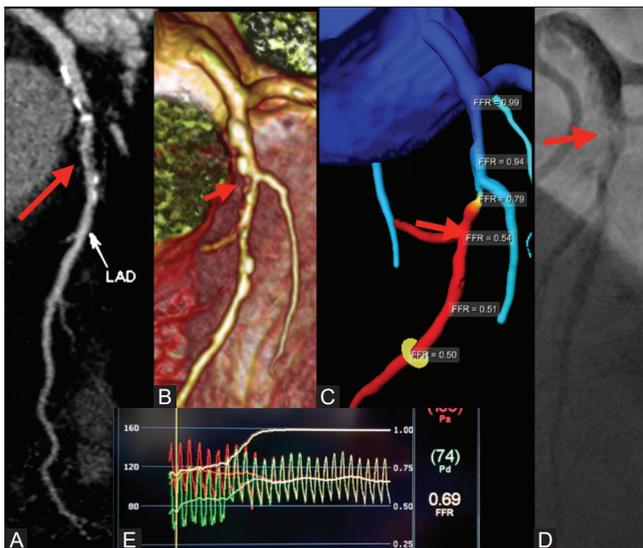


Figure 3 (A-E): (A) CT Angio shows significant disease in proximal LAD, confirmed on VRT (B) CT FFR (C), invasive angio (D), Invasive FFR (E)

the lumen, these segments of the coronary artery are not readable. Obtaining information regarding these segments is possible only by doing additional tests such as myocardial perfusion or invasive catheter angiograms. Fortunately, FFR is not affected by calcium, the FFR at these unreadable segments can be determined so additional tests are not required.

Though CT FFR [Figures 1-4] was FDA approved in 2014, it is unfortunately not widely used as this requires a supercomputer for the computation of CTFRR. CT Angio data has to be sent to an offsite computer for analysis, resulting in a turnaround time which can range from 24 hours to a week. Being a propriety software the cost of data analysis is high ranging from INR 75,000 to 1.25 lacs

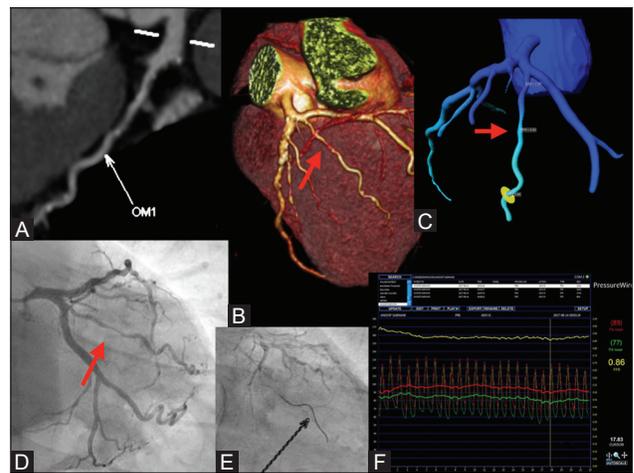


Figure 2 (A-F): (A) CT Angio reveals narrowing in OM1, (B) VRT also demonstrates narrowing, (C) CT FFR reveals narrowing not functionally significant as FFR above 0.8, (D) Catheter angiogram demonstrates narrowing in OM1, (E) Pressure wire beyond narrowing to measure distal pressure, (F) Invasive FFR confirms CT FFR finding of 0.86

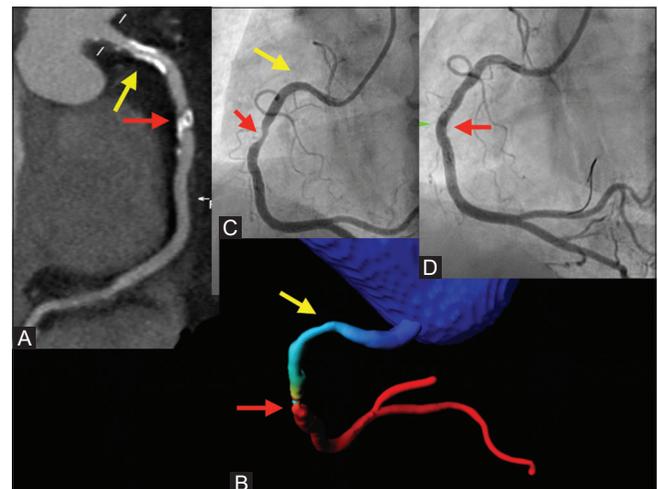


Figure 4 (A-D): (A) CT Angio reveals calcific plaques in proximal RCA narrowing lumen (yellow arrow), Dense calcific plaques in mid RCA obscuring visualisation of lumen (red arrow), (B) CT FFR reveals functional significance of dense plaque, confirmed on invasive cath angio (C) Post angioplasty image (D)

per case! Fortunately, a newer CTFFR technique has been introduced based on deep machine learning using artificial intelligence to compute functional severity of a lesion. In this new model computation time is reduced by 80-fold thus allowing analysis utilizing on site workstations with nearly real time analysis. Numerous studies^[4-6] have compared this new technique with invasive FFR finding it to be accurate. Another useful utility is Virtual stenting, to predict FFR following stenting, how much would flow increase and if any possible residual ischemia.

A combination of CT Anglo and CT FFR provides a mine of information regarding coronary artery disease. With excellent anatomy on CTA, the extent of coronary artery disease is demonstrated. The extent of luminal compromise, focal or diffuse, single or multiple plaques, tended lesions. The morphology of these plaques can be assessed for high risk features. The addition of CT FFR provides information regarding the impact of plaque on blood flow helping to decide further clinical management, especially avoiding unnecessary invasive testing or to guide appropriate revascularization. In fact, the combination of CT Anglo and CTFFR will become the gatekeeper to the invasive cardiac catheterization lab, deciding who needs intervention and who needs medical therapy/lifestyle management or nothing at all!!

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