Coronary CT Angiography-derived Fractional Flow Reserve Testing in Patients with Stable Coronary Artery Disease

Recommendations on Interpretation and Reporting

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Coronary CT Angiography-derived Fractional Flow Reserve Testing in Patients with Stable Coronary Artery Disease: Recommendations on Interpretation and Reporting

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Noninvasive fractional flow reserve derived from coronary CT angiography (FFR_{CT}) is increasingly used in patients with coronary artery disease as a gatekeeper to the catheterization laboratory. While there is emerging evidence of the clinical benefit of FFR_{CT} in patients with moderate coronary disease as determined with coronary angiography, there has been less focus on interpretation, reporting, and integration of FFR_{CT} results into routine clinical practice. Because FFR_{CT} analysis provides a plethora of information regarding pressure and flow across the entire coronary tree, standardized criteria on interpretation and reporting of the FFR_{CT} analysis result are of crucial importance both in context of the clinical adoption and in future research. This report represents expert opinion and recommendation on a standardized FFR_{CT} interpretation and reporting approach.

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Since the first study on coronary CT angiography–derived fractional flow reserve (CT FFR) diagnostic performance by Koo and colleagues in 2011 (1), an abundance of data pertaining to this modality has been published. Several tools have been introduced for the calculation of CT FFR (1–3); however, the majority of existing evidence and clinical experience is based on the HeartFlow FFR_{CT} method (HeartFlow, Redwood City, Calif), which is the only CT FFR cleared by the United States Food and Drug Administration (4) and endorsed by the National Institute for Health and Care Excellence in the United Kingdom (5). Comprehensive reviews of the principle of FFR_{CT} have been described previously (6–8). FFR_{CT} assessment is increasingly used in mainstream clinical practice (9–14) and is likely to further expand with the increased utilization of coronary CT angiography as a first-line test in patients suspected of having coronary artery disease (CAD). While there has been much focus on the diagnostic performance and potential clinical utility of FFR_{CT} in patients with moderate CAD (9–18), there has been less focus on interpretation, reporting, and integration of FFR_{CT} results into routine clinical practice (19). A broadly adopted standardized FFR_{CT} interpretation and reporting approach providing rich and consistent information may facilitate more appropriate clinical implementation and stimulate further high-quality research. Thus, this report, which was written by an independent group of physicians with years of clinical experience with FFR_{CT}, proposes standardized criteria for FFR_{CT} interpretation and reporting for application in clinical practice and for clinical research.

**FFR versus FFR_{CT}**

FFR_{CT} provides simultaneous calculation of pressure and flow across the entire coronary tree (Fig 1). In contrast, information pertaining to invasively measured FFR is only available in vessels that have been interrogated with the pressure wire, which is typically decided during invasive coronary angiography at the discretion of the interventionists (20). While anatomic percentage of stenosis is evaluated at the location of the lesion, invasive FFR is typically measured by positioning the pressure sensor in the distal part of the vessel and then manually pulling the pressure sensor back to the ostium to assess the distribution of abnormal epicardial resistance along the course of the vessel (20). In both invasive FFR and FFR_{CT}, the distal values in any given vessel reflect the cumulative pressure loss and impact of all disease proximal to the measurement location. Values obtained by both techniques may vary depending on the measurement location within a vessel. Accordingly, in vessels that have been assessed using both techniques, if the measurement locations of invasive FFR and FFR_{CT} are not matched, their values can be different and may not closely correlate.
Abbreviations

CAD = coronary artery disease, FFR = fractional flow reserve, FFR\textsubscript{CT} = CT angiography–derived FFR, LAD = left anterior descending artery, SCCT = Society of Cardiovascular Computed Tomography

Summary

Expert opinion and recommendation was given by an independent group of physicians on a standardized interpretation and reporting approach for CT-derived fractional flow reserve testing supported by years of clinical experience.

Key Points

- Standardized criteria on interpretation and reporting of CT-derived fractional flow reserve (FFR\textsubscript{CT}) analysis results are of importance both in context of their clinical adoption and in future research.
- Use of the FFR\textsubscript{CT} value 10–20 mm distal to the lower border of the stenosis for decision making is recommended.
- We recommend for clinical decision making a dichotomous interpretation strategy to be considered only in lesions with FFR\textsubscript{CT} greater than 0.80 or lower than or equal to 0.75, whereas, in patients with FFR\textsubscript{CT} ranging between 0.76 and 0.80, additional risk stratification information is needed.
- The results of FFR\textsubscript{CT} must be evaluated in their clinical context, taking into account patient symptoms, the coronary anatomy, and suitability of revascularization.

FFR\textsubscript{CT} Interpretation

As for CT angiography, FFR\textsubscript{CT} interpretation should be performed by the local imaging experts determined by level of clinical knowledge and practical experience with the technique. This may include cardiologists and/or radiologists. It is recommended that downstream management decision making beyond FFR\textsubscript{CT} takes into account both the clinical scenario (symptoms, risk profile, and/or comorbid conditions) and the coronary anatomy.

Evaluation of CT Angiography and Lesion Location

The first step in the interpretation of FFR\textsubscript{CT} is to re-examine the original coronary CT angiography study with particular focus on the location and severity of detailed anatomic lesions (Table). Because FFR\textsubscript{CT} declines along the length of the vessel with serial focal lesions or areas of diffuse disease, it is important to correlate the pressure loss to specific lesions, which can only be established by direct comparison between the CT angiography lesion location and the FFR\textsubscript{CT} three-dimensional coronary tree model in relation to identifiable vessel landmarks, such as origin, branches, and segments. It is recommended that this first step be performed by using the Society of Cardiovascular Computed Tomography (SCCT) coronary segmentation model (21).

FFR\textsubscript{CT} Threshold

There is high per-patient and per-vessel agreement between FFR\textsubscript{CT} and invasive FFR using the threshold of 0.80 for both techniques (1,15–18). An FFR\textsubscript{CT} value greater than 0.80 indicates that the lesion is unlikely to be hemodynamically significant and that the patient can be safely treated with optimal medical treatment without further downstream testing (1,12–18,22,23). A poststenotic FFR\textsubscript{CT} value less than or equal to 0.80 indicates the possibility of hemodynamic significance (1,15–18). The use of this dichotomous FFR\textsubscript{CT} threshold to guide treatment decisions, namely to avoid further downstream testing or consider invasive angiography and revascularization, remains controversial, as it is well known from the invasive literature that the greatest benefit of revascularization is obtained in patients with the most severe pressure loss (24,25). We recommend a dichotomous interpretation strategy to be considered in lesions with FFR\textsubscript{CT} greater than 0.80 or less than or equal to 0.75 (ie, values >0.80 are “normal” and values ≤0.75 are associated with high likelihood of hemodynamic significance) (Table, Figure 2).

Several factors support this strategy. First, FFR\textsubscript{CT} values are lower than measured FFR (with a bias ranging between 0.03 and 0.05) (16,18). Second, among patients with FFR\textsubscript{CT} values less than or equal to 0.80, there is a graded correlation between FFR\textsubscript{CT} and invasive FFR, with the highest FFR\textsubscript{CT} uncertainty in the range between 0.76 and 0.80 and the highest agreement when FFR\textsubscript{CT} is less than or equal to 0.75 (12,18). Third, FFR\textsubscript{CT} similar to FFR, exhibits a continuous relationship between its numerical value and clinical outcomes, with the worst outcome at lower FFR\textsubscript{CT} values (14,22,23). Finally, symptomatic patients with moderate CAD determined at CT angiography and FFR\textsubscript{CT} values greater than 0.80 and in whom invasive angiography is deferred have a favorable prognosis (12,14,22,23).

Clinical decision making in patients with FFR\textsubscript{CT} ranging between 0.76 and 0.80 is nuanced and may benefit from consideration of additional risk stratification information (Fig 2). Identifying patients at incrementally higher cardiovascular risk, who may benefit from an early coronary angiography approach, can be done by assessing several factors: high-risk plaque features (low attenuation, positive remodeling, napkin-ring sign) (26–28), plaque burden (27,28), stenosis location (proximal vs distal; main vessel vs side branch) (25,29,30), vessel territory (left anterior descending artery [LAD] vs non-LAD) (29), ratio of coronary vessel volume to myocardial mass (31), and/or the translesional FFR\textsubscript{CT} gradient (ΔFFR\textsubscript{CT}) (32). It is the opinion of the present author group that in certain instances with FFR\textsubscript{CT} values less than or equal to 0.75 (eg, small vessels, distal lesions, side branches), patients may be treated with optimal medical therapy without referral to invasive angiography as a first-line strategy (14,33).

In a recent retrospective study, a large pressure drop (ΔFFR\textsubscript{CT} ≥ 0.06) was a stronger predictor of culprit lesions for future acute coronary syndromes than FFR\textsubscript{CT} measured distal to the lesion alone (32). Ongoing studies are assessing the potential diagnostic value of ΔFFR\textsubscript{CT} in clinical practice. Overall, the results of FFR\textsubscript{CT}, as for invasive FFR, must always be evaluated in their clinical context, taking into account patient symptoms and comorbid conditions, which inform the goals of coronary intervention, in combination with the coronary anatomy and suitability of revascularization.
the lesion did not cause significant pressure loss. However, FFRCT was significantly low (0.76) in the terminal vessel segments.

In patients with CAD, as for measured FFR, FFRCT values decline from the ostium to the distal vessel irrespective of the vessel territory, stenosis severity, and location (14,19,34–36). In FFR practice, it is advised that the FFR value within the throat of the lesion (which may correspond to the minimum FFRCT value) is not used clinically and that the pressure is assessed at least 2–3 cm distal to the stenosis of interest (20). Likewise, for clinical decision making, we recommend using the FFRCT value 1–2 cm distal to the lower border of the stenosis, avoiding the pressure recovery phenomenon.

**Distal Vessel FFRCT Values**

FFRCT provides simultaneous computation of pressure and flow in the entire coronary tree, thus exposing both lesion-specific pressure as well as nadir FFRCT values across the coronary system, which in various settings may drop less than or equal to 0.80 (14,19,34–36) (Fig 1). Low terminal vessel FFRCT values (rather than a value distal to stenosis) may include effects unrelated to the stenosis (19,35–37). These low values remote from a focal lesion may be due to diffuse CAD or reflect the sum of serial flow-limiting lesions (35–37). In recent studies, 35%–44% of patients with stable CAD and terminal vessel FFRCT values less than or equal to 0.80 were reclassified as negative when the FFRCT point of reading was 1–2 cm distal to stenosis (14,35). In one observational single-center study, the intermediate follow-up clinical outcome was favorable in patients with terminal FFRCT values less than or equal to 0.80 who were treated with optimal medical treatment (14). In vessels without a significant pressure loss within 2 cm distal to the lesion of interest, but with FFRCT values less than or equal to 0.80 in nearby (eg, mid coronary) segments, we recommend assessment for extent of upstream disease including both CT angiography and FFRCT. FFRCT values less than or equal to 0.80 in such circumstances may be clinically relevant (especially when present distal to a lesion in a proximal segment supplying a large myocardial territory). The group recognizes that more research is needed, particularly in large vessels that have discordance between lesion-specific FFRCT and values taken 2 cm beyond an upstream lesion.

**Serial Lesions**

The individual contribution of a given lesion in the event of serial stenosis cannot be assessed with FFRCT similar to measured FFR, in any straightforward way because of the complex physiologic interplay between stenoses (Fig 3). At present, there is no accepted way to identify the lesion that contributes most to this cumulative pressure loss. Intuitively, the intrinsic impact of a given lesion should relate to ΔFFRCT of that individual lesion, and previous data have in fact demonstrated excellent correlation between ΔFFRCT and invasive ΔFFR (38). However, in a recent study, it was demonstrated that ΔFFRCT (as well as ΔFFR) may underestimate the physiologic contribution of stenosis in vessels with serial lesions (39). An interactive revascularization FFRCT-based planner tool (HeartFlow) may more accurately predict the invasive FFR contribution of each stenosis in serial CAD (39). The

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**Figure 1:** (a) Interpretation of FFRCT results in a 65-year-old woman with typical angina. Agatston score, 333. Left: Coronary CT angiography curved multiplanar reconstructions demonstrate a 50%–69% proximal left anterior descending artery (LAD) stenosis (red arrow) and in the mid-LAD, nonobstructive diffuse disease. The blue arrow indicates where the lesion-specific FFRCT value was assessed. Right: In the FFRCT three-dimensional model, the FFRCT value 16 mm distal to the stenosis was 0.85, indicating that the lesion did not cause significant pressure loss. However, FFRCT was significantly low (0.76) in the terminal vessel segments. (b) Interpretation of FFRCT results in a 63-year-old man with atypical angina. Agatston score, 245. Left: Coronary CT angiographic images demonstrate a 50%–69% proximal LAD stenosis (red arrow). The blue arrow indicates where the lesion-specific FFRCT value was assessed. Right: In the FFRCT three-dimensional model, the FFRCT value 14 mm distal to the stenosis indicated that the lesion was hemodynamically significant with a value of 0.69. Coronary CT angiography and FFRCT reporting are demonstrated in Figure 4. LCX = left circumflex coronary artery, RCA = right coronary artery.

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**Standardized Interpretation of Hemodynamically Significant Lesions**

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ongoing Precise Percutaneous Coronary Intervention plan (P3) study (ClinicalTrials.gov: NCT03782688) investigates the diagnostic value of the FFR<sub>CT</sub> revascularization planner tool.

**FFR<sub>CT</sub> Reporting**

Coronary CT angiography and FFR<sub>CT</sub> uniquely provide simultaneous anatomic and functional information in a noninvasive fashion. To provide useful, actionable guidance for medical or invasive management, the FFR<sub>CT</sub> report must relate the observed anatomic coronary CT angiography findings with lesion-specific FFR<sub>CT</sub> values. The principal purpose of the report is to communicate these findings and their clinical implications (Fig 4).

**Indications**

The indications for the FFR<sub>CT</sub> analysis should include clinical information from the original coronary CT angiography report, as well as specific anatomic details from the impression of the report that motivated the performance of FFR<sub>CT</sub> analysis. Mention should be made of factors pertinent to the FFR<sub>CT</sub> indication and suitability for analysis, such as angiographic degree of stenosis, extent of calcifications, and overall image quality (signal-to-noise ratio, motion artifacts, luminal contrast opacification). The indications should specify the anatomic lesions from the original coronary CT angiography report that were of particular concern in ordering the FFR<sub>CT</sub> analysis. The present author group finds FFR<sub>CT</sub> testing appropriate in patients with intermediate anatomic stenosis. FFR<sub>CT</sub> values may be less than or equal to 0.80 in lesions of less than 50% diameter stenosis. Physiologic characterization with FFR<sub>CT</sub> may be relevant in a small proportion of such lesions when located in proximal coronary segments supplying a large myocardial territory because they may have prognostic implications (40). On the other hand, even high-grade anatomic lesions with stenosis severity greater than 70% or even greater than 90%, which are generally considered flow limiting, may overestimate the physiologic significance (41,42). Therefore, we commonly use FFR<sub>CT</sub> testing in the setting of more severe anatomic disease and multivessel disease to help guide decision making on downstream catheterization and potential revascularization planning (Fig 2). As with any test, the appropriateness is often determined on a case-by-case basis and commonly related to many factors beyond stenosis severity (Fig 2). Finally, because the impact of coronary occlusion on the diagnostic performance of FFR<sub>CT</sub> is unknown, we do not recommend FFR<sub>CT</sub> analysis to be prescribed in such circumstances.

### Summary FFR<sub>CT</sub> Values

| Value | Interpretation                  |
|-------|--------------------------------|
| > 0.80| Not hemodynamically significant|
| 0.76–0.80| Borderline hemodynamically significant|
| ≤ 0.75| Hemodynamically significant  |

**Approach to Interpreting FFR<sub>CT</sub> Values**

- **No additional testing**
  - **Assess**
    - High risk plaque features
    - Plaque burden
    - No of vessels with stenosis
    - Stenosis location
    - ΔFFR<sub>CT</sub>
  - **Consider invasive angiography**

**Figure 2**: FFR<sub>CT</sub> 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. Anatomic characteristics beyond stenosis severity, patient symptoms, and suitability of revascularization may influence decisions on management after coronary CT angiography (CTA). ** = Posttest risk stratification: Test results must always be evaluated in their clinical context, taking into account patient symptoms and preferences as well as high-risk anatomic features and likelihood of revascularization.

**Results**

We recommend FFR<sub>CT</sub> values to be reported for each major coronary branch by specific coronary segments (diameter greater than 1.8 mm) using the standardized SCCT guidelines for coronary segmentation classification (21), and that the values be related to specific lesions within a given segment. Any lesion identified in the original coronary CT angiography report as a potential source of pressure loss should be specifically reported in the FFR<sub>CT</sub> report and its standard SCCT coronary segment identified. A given FFR<sub>CT</sub> value may have different therapeutic implications if located in a proximal segment as opposed to either a distal location or within a minor side branch (25,29,30). If no FFR<sub>CT</sub> value
of 0.80 or less was reported in a given artery territory, we recommend the lowest value for that territory be reported. It is not necessary to provide FFR_{CT} values greater than 0.80 for minimal (1%–24% stenosis) or mild (25%–49%) lesions unless located in the left main or proximal LAD or when containing high-risk plaque features, in which case FFR_{CT} values should be provided. Any lesion with an abnormal FFR_{CT} value should be reported even if not considered as a likely source of significant pressure loss in the original coronary CT angiography report. We recommend that an FFR_{CT} value be provided for all moderate (50%–69%) and all severe (>70% to 99%) stenoses.

FFR_{CT} values 0.80 or lower that are measured more than 2 cm beyond a lesion not causing a significant focal pressure loss (FFR_{CT} > 0.80) should be reported when present in large vessels. The clinical significance of FFR_{CT} values 0.80 or lower in the distal coronary tree remote from any focal lesion is unknown. These may be reported; however, it should be stated that the values are remote from angiographic stenosis and are of uncertain clinical significance.

In the event of serial lesions, we recommend that the value of FFR_{CT} 10–20 mm distal to each lesion should be reported. If this is not possible, FFR_{CT} values between lesions should be reported, including information on the distance between stenosis and the FFR_{CT} value.

Occlusion of small vessels that were overlooked in the primary CT angiography assessment (typically involving distal segments or small side branches) may be revealed by the FFR_{CT} analysis process. While this may or may not be clinically relevant, an occluded branch may have some slight impact on FFR_{CT} in the parent vessel. The impact will depend on the size of the branch relative to other vessels. Occluded segments should be identified and referenced.

In recognition of the fact that FFR_{CT} is a mathematically derived analysis rather than an actual measurement of flow and pressure, it is recommended that results be described as demonstrating low, borderline, or high likelihood of hemodynamic significance rather than ischemia (Table).

**Impression**

The report summary should focus on the presence of a low, borderline, or high likelihood of hemodynamic significance of the lesions identified in the impression section of the original coronary CT angiography report. In addition, any other lesion that has a borderline or high likelihood of hemodynamic significance should be reported even if it was not identified in the original coronary CT angiography interpretation. In particular, areas of diffuse coronary disease that produce low FFR_{CT} values distal to the affected segments should be described.

**Format**

It is recognized that institutional requirements may dictate the specific reporting format required. Ideally, the coronary CT angiography and FFR_{CT} reports can be combined into a single uniform report that will most clearly relate anatomic and functional information. However, it is important to interrogate the anatomy to assess the extent and severity of CAD to determine the need for FFR_{CT} analysis. Given the time gap between the coronary CT angiography and FFR_{CT} results, either a preliminary CT angiography report may be finalized after the FFR_{CT} results are available or an FFR_{CT} report may subsequently be added to the original coronary CT angiography report. Both of these formats closely incorporate the most detailed description of anatomy and functional significance with minimal repetition. If institutions require a separate free-standing report, additional details in the indications should be provided to emphasize the severity, morphology, and location of lesions suspected of causing flow limitation.

**FFR_{CT} Images**

It is recommended that relevant images from the FFR_{CT} report should be included if technically possible to more accurately convey the location of FFR_{CT} values at a specific anatomic location. This will help other physicians understand the location and extent of the pressure loss and the location for potential confirmatory invasive FFR measurement and will facilitate medical or invasive treatment planning. Providing images combining FFR_{CT} values and their specific location can rapidly and succinctly convey the extent of pressure loss and facilitate therapeutic decision making more easily than if textual description was offered alone.

**Management Recommendations**

The decision of whether FFR_{CT} interpretation reports should contain management recommendations (ie, consideration for...
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**CTA:**
Indications: Typical chest pain, family history of premature CAD.

Protocol: Patient education was provided. 100 mg atenolol followed by intravenous metoprolol (a total of 15 mg), and 0.8 mg of spray sublingual nitroglycerin were administered. Images were obtained using a dual-source 128-slice CT scanner following the rapid IV infusion of 60 ml of contrast.

Image quality: Good. CTA does not permit accurate assessment of vessels equal to or less than 1.5 mm in diameter. Vessels designated as normal are without visible disease within the limitations of the CTA technique.

**Coronary anatomy:**
Agatston score = 245
Left main: 1-24% non-calcified plaque stenosis.
Left anterior descending artery (LAD): Segment 6 with diffuse CAD including both non-calcified and calcified plaques. 50-69% mixed complex plaque stenosis. In more distal segments and side-branches stenosis severity <24%.
Left circumflex artery (LCX): No CAD detected.
Right coronary artery (RCA): Segment 2 with a non-calcified positively remodeled plaque with 30-49% stenosis. Right dominance.

**Noncoronary cardiac findings:**
1. The aorta shows no calcification, dilatation or dissection.
2. The pulmonary artery shows no dilatation or thrombus.
3. The pericardium shows no effusion, thickening or calcification.
4. No extra-cardiovascular abnormal findings present.

**Impression:**
+ CAD. Proximal LAD 50-69% complex mixed plaque stenosis. Mid-RCA stenosis of borderline significance. Further evaluation with $\text{FFR}_{CT}$ was prescribed.

**$\text{FFR}_{CT}$ Report:**

![Image of coronary CT angiography–$\text{FFR}_{CT}$ report](patient case, Fig 1b). CAD = coronary artery disease, CTA = coronary CT angiography.

LAD: Segment 6: There is a high likelihood of hemodynamic significance with an $\text{FFR}_{CT}$ value of 0.69.
LCX: No anatomically disease.
RCA: Low likelihood of hemodynamic significance with the lowest value in the terminal segments of 0.93.

**Impression:** Proximal LAD stenosis with high likelihood of hemodynamic significance.

**Figure 4:** Example of a coronary CT angiography–$\text{FFR}_{CT}$ report (patient case, Fig 1b). CAD = coronary artery disease, CTA = coronary CT angiography.
invasive coronary angiography or optimal medical therapy alone) will be determined by local institutional practices. If management recommendations are typically included in reports, note should be made that FFR values should not be considered in isolation but are integrated with clinical and other imaging factors such as symptoms, plaque morphology, and lesion location. This is particularly important in cases of borderline FFR values between 0.76 and 0.80 (Fig 2).

**Limitations**

The diagnostic performance and utility of FFR has been studied only in patients suspected of having stable CAD. At present, the use of FFR in patients with stents or bypass grafts, microvascular dysfunction, prior myocardial infarction, or suspected or known acute coronary syndromes cannot be recommended. FFR analysis cannot be performed in all patients. Coronary CT angiography–related artifacts, such as motion, misalignment, low contrast, or blooming from coronary calcification, may impair the diagnostic reliability of CT angiography and FFR (43–45). It is our experience that FFR has high diagnostic performance in patients with coronary calcification. However, our experience with FFR testing in patients with severe calcification (Agatston score > 1000) is limited, and in two previous studies demonstrating high diagnostic performance of FFR in vessels and patients with high calcium scores, the number of such patients were low (44,45). In previous multicenter studies of FFR, diagnostic performance, CT angiographic images were not of sufficient quality for FFR, analysis in 11%–13% of patients (15,16), whereas in more recent single-center studies that assessed the clinical utility of FFR less than 4% of the patients did not meet the image quality requirements (10–12,14).

**Conclusion**

By virtue of the complexity of the FFR analysis providing information on pressure and flow across the entire coronary tree, standardized criteria on interpretation and reporting of the FFR analysis results are of crucial importance both in context of clinical adoption of the test and in future research. For assessment of the hemodynamic significance of lesions, we recommend using the FFR value 10–20 mm distal to the lower border of the stenosis. For clinical decision making, we recommend a dichotomous interpretation strategy be considered only in lesions with FFR greater than 0.80 or less than or equal to 0.75, whereas in patients with FFR ranging between 0.76 and 0.80, additional risk stratification information is needed. The results of FFR must always be evaluated in their clinical context, taking into account patient symptoms, the coronary anatomy, and suitability of revascularization.

**Author contributions:** Guarantees of integrity of entire study, B.L.N., M.G.R.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, B.L.N., T.A.F., R.D.S., M.G.R., B.K., K.N., N.P.S., H.M., J.L.; clinical studies, R.D.S., M.G.R., B.K., N.P.S., H.M., J.L.; statistical analysis, B.L.N., B.K., N.P.S.; and manuscript editing, all authors

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**References**

1. Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. J Am Coll Cardiol 2011;58(19):1989–1997.
2. Goen a N, Lübbers MM, Kurata A, et al. Fractional flow reserve computed from noninvasive CT angiography data: diagnostic performance of an on-site clinician-operated computational fluid dynamics algorithm. Radiology 2015;274(3):674–683.
3. Ko BS, Cameron JD, Munnur RK, et al. Noninvasive CT-derived FFR based on structural and fluid analysis: a comparison with invasive FFR for detection of functionally significant stenosis. JACC Cardiovasc Imaging 2017;10(6):663–673.
4. U.S. Food and Drug Administration. 510(k) Premarket Notification. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm . Accessed November 12, 2019.
5. National Institute for Health and Care Excellence. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. Clinical guideline CG95. London: NICE, 2016. https://www.nice.org.uk/guidance/CG95. Accessed November 12, 2019.
6. Zarins CK, Taylor CA, Min JK. Computed fractional flow reserve (FFCT) derived from coronary CT angiography. J Cardiovasc Transl Res 2013;6(5):708–714.
7. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve: scientific basis. J Am Coll Cardiol 2013;61(22):2333–2341.
8. Min JK, Taylor CA, Achenbach S, et al. Noninvasive fractional flow reserve derived from coronary CT angiography: Clinical data and scientific principles. JACC Cardiovasc Imaging 2015;8(10):1209–1222.
9. 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 impact study. Eur J Heart J 2015;36(47):3359–3367.
10. Nørgaard BL, Gormsen LC, Bøtke r HE, et al. Myocardial perfusion imaging versus computed tomography angiography-derived fractional flow reserve testing in stable patients with intermediate-range coronary lesions: influence on downstream diagnostic workflows and invasive angiography findings. J Am Heart Assoc 2017;6(8):e005587.
11. Jensen JM, Berker HE, Mathiasen ON, et al. Computed tomography derived fractional flow reserve testing in stable patients with typical angina pectoris.
influence on downstream rate of invasive coronary angiography. Eur Heart J Cardiovasc Imaging 2018;19(4):405–414.

12. Norgaard BL, Hjort J, Gaur S, et al. Clinical use of coronary CTA-derived FFR for decision-making in stable CAD. JACC Cardiovasc Imaging 2017;10(5):541–550.

13. Fairbairn TA, Nieman K, Akasaka T, et al. 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(44):3701–3711.

14. Norgaard BL, Terkelsen CJ, Mathiasen ON, et al. Coronary CT angiographic and flow reserve-guided management of patients with stable ischemic heart disease. J Am Coll Cardiol 2018;72(18):2123–2134.

15. Min JK, Leipsic J, Pencina MJ, et al. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. JAMA 2012;308(12):1237–1245.

16. Norgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). J Am Coll Cardiol 2014;63(12):1145–1155.

17. Sand NPR, Veien KT, Nielsen SS, et al. Prospective comparison of FFR derived from coronary CT angiography with SPECT perfusion imaging in stable coronary artery disease: the ReASSess study. JACC Cardiovasc Imaging 2018;11(11):1640–1650.

18. Driessen RS, Danai I, Stuijfzand WJ, et al. Comparison of coronary computed tomography angiography, fractional flow reserve, and perfusion imaging for ischemia diagnosis. J Am Coll Cardiol 2019;73(2):161–173.

19. Rabbat MG, Berman DS, Kern M, et al. Interpreting results of coronary computed tomography angiography-derived fractional flow reserve in clinical practice. J Cardiovasc Comput Tomogr 2017;11(5):383–388.

20. Toth GG, Johnson NP, Jermias A, et al. Standardization of Fractional Flow Reserve Measurements. J Am Coll Cardiol 2016;68(7):742–753.

21. Leipsic J, Abbasra S, Achenbach S, et al. SCCT guidelines for the interpretation and reporting of coronary CT angiography: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee. J Cardiovasc Comput Tomogr 2014;8(5):342–358.

22. Patel MR, Norgaard BL, Fairbairn TA, et al. 1-Year Impact on Medical Practice and Clinical Outcomes of FFRCT: The ADVANCE Registry. JACC Cardiovasc Imaging 2019 Mar 17 [Epub ahead of print].

23. Ildayhid AR, Norgaard BL, Gaur S, et al. Prognostic value and risk continuum of noninvasive fractional flow reserve derived from coronary CT angiography. Radiology 2019;292(2):343–351.

24. Johnson NP, Toth GG, Lai D, et al. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. J Am Coll Cardiol 2014;64(16):1641–1654.

25. Adjej J, De Bruiyne B, Floré V, et al. Significance of intermediate values of fractional flow reserve in patients with coronary artery disease. Circulation 2016;133(5):502–508.

26. Motoyama S, Itou H, Sarai M, et al. Plaque characterization by coronary computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up. J Am Coll Cardiol 2015;66(4):337–346.

27. Park HB, Heo R, H Hartarigh B, et al. Atherosclerotic plaque characteristics by CT angiography identify coronary lesions that cause ischemia: a direct comparison to fractional flow reserve. JACC Cardiovasc Imaging 2015;8(1):1–10.

28. Gaur S, Øvrehus KA, Dey D, et al. Coronary plaque quantification and fractional flow reserve by coronary computed tomography angiography identify ischaemia-causing lesions. Eur Heart J 2016;37(15):1220–1227.

29. Kim HY, Lim HS, Doh JH, et al. Physiological severity of coronary artery stenosis depends on the amount of myocardial mass subtended by the coronary artery. JACC Cardiovasc Imaging 2016;9(15):1548–1560.

30. Kim HY, Doh JH, Lim HS, et al. Identification of coronary artery side branch supplying myocardial mass that may benefit from revascularization. JACC Cardiovasc Imaging 2017;10(6):571–581.

31. Taylor CA, Gaur S, Leipsic J, et al. Effect of the ratio of coronary arterial lumen volume to left ventricle myocardial mass derived from coronary CT angiography on fractional flow reserve. J Cardiovasc Comput Tomogr 2017;11(6):429–436.

32. 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;12(6):1032–1043.

33. Norgaard BL, Jensen JM, Blanke P, Sand NP, Rabbat M, Leipsic J. Coronary CT angiography-derived fractional flow reserve: the game changer in noninvasive testing. Curr Cardiol Rep 2017;19(11):112.

34. Takagi H, Ishikawa Y, Oriti M, et al. Optimized interpretation of fractional flow reserve derived from computed tomography: Comparison of three interpretation methods. J Cardiovasc Comput Tomogr 2019;13(2):134–141.

35. Kueh SH, Mooney J, Ohana M, et al. Fractional flow reserve derived from coronary computed tomography angiography reclassification rate using value distal to lesion compared to lowest value. J Cardiovasc Comput Tomogr 2017;11(6):462–467.

36. Cami E, Tagami T, Raff G, et al. Assessment of lesion-specific ischemia using fractional flow reserve (FFR) profiles derived from coronary computed tomography angiography (FFRCT) and invasive pressure measurements (FFRNV): importance of the site of measurement and implications for patient referral for invasive coronary angiography and percutaneous coronary intervention. J Cardiovasc Comput Tomogr 2018;12(6):480–492.

37. De Bruiyne B, Hershback F, Pijs NH, et al. Abnormal epicardial coronary resistance in patients with diffuse atherosclerosis but “Normal” coronary angiography. Circulation 2001;104(20):2401–2406.

38. Tanaka K, Bezerra HG, Gaur S, et al. Comparison between non-invasive (coronary computed tomography angiography derived) and invasive-fractional flow reserve in patients with serial stenoses within one coronary artery: a NXT Trial substudy. Ann Biomed Eng 2016;44(2):580–589.

39. Modi BN, Sankaran S, Kim HJ, et al. Predicting the physiological effect of revascularization in serially diseased coronary arteries. Circ Cardiovasc Inter 2019;12(2):e007577.

40. Toth G, Hamilos M, Pyxaras S, et al. Evolving concepts of angiogram: fractional flow reserve discordances in 4000 coronary stenoses. Eur Heart J 2014;35(40):2831–2838.

41. Layland J, Oldroyd KG, Curzen N, et al. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS-NSTEMI randomized trial. Eur Heart J 2015;36(2):100–111.

42. Curzen N, Rana O, Nicholas Z, et al. Does routine pressure wire assessment influence management strategy at coronary angiography for diagnosis of chest pain?: the RIPCORD study. Circ Cardiovasc Inter 2014;7(2):248–255.

43. Leipsic J, Yang TH, Thompson A, et al. CT angiography (CTA) and diagnostic performance of noninvasive fractional flow reserve: results from the Determination of Fractional Flow Reserve by Anatomic CTA (DeFACTO) study. AJR Am J Roentgenol 2014;202(5):989–994.

44. Min JK, Koo BK, Englis A, et al. Effect of image quality on diagnostic accuracy of noninvasive fractional flow reserve: results from the prospective multicenter international DISCOVER-FLOW study. J Cardiovasc Comput Tomogr 2012;6(3):191–199.

45. Norgaard BL, Gaur S, Leipsic J, et al. Influence of coronary calcification on the diagnostic performance of CT angiography derived FFR in coronary artery disease: A study of the NXT trial. JACC Cardiovasc Imaging 2015;8(9):1045–1055.