Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Impact of Fractional Flow Reserve Derived From Coronary Computed Tomography Angiography on Heart Team Treatment Decision-Making in Patients With Multivessel Coronary Artery Disease

Insights From the SYNTAX III Revolution Trial

AQ1

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BACKGROUND: Fractional flow reserve (FFR) is a reliable tool for the functional assessment of coronary stenoses. FFR computed tomography (CT) derived (FFR_{CT}) has shown to be accurate, but its clinical usefulness in patients with complex coronary artery disease remains to be investigated. The present study sought to determine the impact of FFR_{CT} on heart team's treatment decision-making and selection of vessels for revascularization in patients with 3-vessel coronary artery disease.

METHODS: The trial was an international, multicenter study randomizing 2 heart teams to make a treatment decision between percutaneous coronary interventions and coronary artery bypass grafting using either coronary computed tomography angiography or conventional angiography. The heart teams received the FFR_{CT} and had to make a treatment decision and planning integrating the functional component of the stenoses. Each heart team calculated the anatomic SYNTAX score, the noninvasive functional SYNTAX score and subsequently integrated the clinical information to compute the SYNTAX score III providing a treatment recommendation, that is, coronary artery bypass grafting, percutaneous coronary intervention, or equipoise coronary artery bypass grafting-percutaneous coronary intervention. The primary objective was to determine the proportion of patients in whom FFR_{CT} changed the treatment decision and planning.

RESULTS: Overall, 223 patients were included. Coronary computed tomography angiography assessment was feasible in 99% of the patients and FFR_{CT} analysis in 88%. FFR_{CT} was available for 1030 lesions (mean FFR_{CT} value 0.64±13). A treatment recommendation of coronary artery bypass grafting was made in 24% of the patients with coronary computed tomography angiography with FFR_{CT}. The addition of FFR_{CT} changed the treatment decision in 7% of the patients and modified selection of vessels for revascularization in 12%. With conventional angiography as reference, FFR_{CT} assessment resulted in reclassification of 14% of patients from intermediate and high to low SYNTAX score tertile.

CONCLUSIONS: In patients with 3-vessel coronary artery disease, a noninvasive physiology assessment using FFR_{CT} changed heart team's treatment decision-making and procedural planning in one-fifth of the patients.

VISUAL OVERVIEW: A visual overview is available for this article.

CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT02813473. AQ3

Key Words: angiography ■ coronary artery disease ■ coronary computed tomography angiography ■ decision-making ■ percutaneous coronary intervention AQ4

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WHAT IS KNOWN

- The SYNTAX III Revolution trial showed that in patients with 3-vessel coronary artery disease treatment decision-making based on coronary computed tomography angiography is in high agreement with the decision derived from conventional angiography.
- Physiology-guided (invasive fractional flow reserve [FFR]) percutaneous coronary revascularization has been associated with lower rate of MACE compared with invasive angiographic guidance and is recommended by the latest guidelines. AQ5

WHAT THE STUDY ADDS

- The heart team changed the treatment recommendation in 7% of the cases and modified the selection of vessels to be revascularized in 12% when functional evaluation with FFR_{CT} was added to an anatomic assessment with coronary computed tomography angiography alone.
- In patients assessed by coronary computed tomography angiography, FFR_{CT} reduced the proportion of patients with hemodynamically significant 3-vessel coronary artery disease from 92.3% to 78.8% and reclassified to a lower SYNTAX Score 15.5% of patients.

Nonstandard Abbreviations and Acronyms

CABG	coronary artery bypass grafting
CAD	coronary artery disease
CTA	coronary computed tomography angiography
FAME	Fractional Flow Reserve Versus Angiography for Multivessel Evaluation
FFR	fractional flow reserve
FFR_{CT}	fractional flow reserve derived from computed tomography
PCI	percutaneous coronary interventions

Revascularization by either percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) is indicated in flow-limiting coronary stenoses to reduce myocardial ischemia and its adverse clinical manifestations.[1] In patients with multivessel coronary artery disease (CAD), physiology-guided coronary revascularization has shown to improve clinical outcomes compared with an angiographic assessment alone.[2] Determination of pressure-wire indexes such as fractional flow reserve (FFR) or instantaneous wave-free ratio has demonstrated that almost half of the lesions with a diameter stenosis >50% are not hemodynamically significant.[3]

FFR derived from computed tomography angiography (FFR_{CT}) is a noninvasive method able to identify lesion-specific ischemia. In patients with multivessel disease, FFR_{CT} has shown to have good diagnostic performance with invasive pressure-wire assessment as reference.[4] Moreover, the extent, severity, and functional component of CAD can be objectively quantified using the functional SYNTAX score.[4] The functional SYNTAX score has higher discrimination for clinical events compared with the anatomic SYNTAX score, while reducing inter-observer variability. The calculation of the SYNTAX score III, combining in a noninvasive setting anatomy, physiology and patient's clinical information provides the heart team with individualized risk stratification and treatment recommendation based on the predicted 4-year mortality in patients undergoing PCI or CABG.[5]

The SYNTAX III Revolution trial showed that in patients with left main or 3-vessel CAD treatment decision-making based on coronary computed tomography angiography (CTA) is in high agreement with the decision derived from conventional angiography.[6] However, the influence of FFR_{CT} on treatment decision-making and selection of vessels for revascularization remains to be investigated. Thus, the present study sought to determine the impact of FFR_{CT} on heart team's treatment decision and procedural planning in patients with left main or 3-vessel CAD.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Design

The present study reports the secondary end point of the SYNTAX III REVOLUTION trial. The design of the SYNTAX III REVOLUTION Trial, a randomized study investigating the use of CT scan and angiography of the heart to help the doctors decide which method is the best to improve blood supply to the heart in patients with complex coronary artery disease, has been reported previously.[5] The trial was an international, multicenter study randomizing 2 heart teams to make a treatment decision between PCI and CABG using either coronary CTA or conventional angiography, while blinded to the other imaging modality. The results of the primary end point based on coronary anatomy alone have been recently published.[6] The present analysis focuses on a second level of the 2 heart teams decision-making after the incorporation of the physiology component (FFR_{CT}) in the coronary CTA diagnostic strategy arm, which represents the secondary end point of the SYNTAX III REVOLUTION trial.[5] The study was approved by an institutional review committee, and the subjects gave informed consent. The European Cardiovascular Research Institute (Rotterdam, the Netherlands) with unrestricted grants from GE Healthcare (Chicago, IL) and Heart Flow Inc (Redwood City, CA) sponsored the study. AQ6

Enrolment and Randomization

Patients with left main or 3-vessel CAD diagnosed with either coronary CTA or conventional angiography and candidates for either PCI or CABG were assessed for eligibility. Patients were consented to undergo coronary CTA using a whole-heart coverage, high-definition CT scanner (Revolution CT; GE Healthcare, Chicago, IL), and to participate in a randomized trial of decision-making between PCI and CABG performed by the local heart team and relying on alternative imaging techniques. Two heart teams composed by an interventional cardiologist, a cardiac surgeon and a radiologist specialized in cardiac imaging, were randomized to either assess the coronary anatomy with coronary CTA or conventional angiography in addition to the patient's clinical information. The heart team allocated to coronary CTA had to make a second treatment decision and procedural planning taking into consideration the functional component of the coronary stenoses provided by FFR_{CT}. Similarly, the heart team randomized to conventional angiography received coronary CTA with FFR_{CT} and had to make a second treatment decision based on the 3 diagnostic methods. Each heart team calculated the anatomic SYNTAX score based only on their allocated imaging modality, the noninvasive functional SYNTAX score, and subsequently integrated the clinical information to compute the SYNTAX score III providing a treatment recommendation, that is, CABG, PCI, or equipoise between CABG and PCI. Any anatomic SYNTAX score was eligible for screening, and patients with anatomic SYNTAX score >33 were not excluded. Patients with prior revascularization were excluded. Complete details of the inclusion and exclusion criteria have been previously described.[5,6]

Image Acquisition and Analysis

Coronary CTA was performed with the GE Revolution CT scanner.[7] A proprietary post-processing algorithm (Snap Shot Freeze) allowed for the correction of motion artifacts.[8] The imaging acquisition guidelines are detailed in the Table I in the Data Supplement. Image quality was assessed using the 5-point Likert scale at the patient level. The 2 local heart teams signed off their decision on the choice of revascularization mode based on the anatomic assessment alone. Subsequently, the FFR_{CT} was used to calculate the noninvasive functional SYNTAX score, computed by subtracting nonflow limiting stenoses (FFR_{CT} >0.80) from the anatomic SYNTAX score. FFR_{CT} has a lower limit of detection of 0.50. Finally, the noninvasive functional SYNTAX score was used to calculate the SYNTAX Score III, which is conceptually a combination of coronary anatomy complexity with its functional repercussion and patient's clinical characteristics and comorbidities. The anatomic and functional SYNTAX scores were also calculated by an independent core laboratory (Cardialysis BV, Rotterdam, the Netherlands) and were made available to each heart team for consultation. For the present article, the functional SYNTAX score was calculated from the heart team assessment, whereas lesion level data were analyzed by the core laboratory (Cardialysis BV, Rotterdam, the Netherlands).

Objectives

The primary objective of the present study was to determine the proportion of patients in whom FFR_{CT} changed the treatment decision and the selection of vessels for revascularization with respect to the management based on anatomic assessment with either coronary CTA or conventional angiography. The secondary objective was to assess the impact of FFR_{CT} on patients risk reclassification compared to the anatomic assessment alone using the SYNTAX score tertiles (SYNTAX score: 0–22, 23–32, and >32).

Statistical Analysis

The heart team's treatment recommendation led to one of 3 decisions according to the SYNTAX Score III: (1) CABG only, patients should be treated by CABG due to a higher 4-year mortality with PCI; (2) PCI only, patients should be treated by PCI due to a higher 4-year mortality with CABG; and (3) equipoise between CABG and PCI, patients could be treated by either approach, considering that the 4-year mortality prediction is similar between them. The power calculation of the sample size of the SYNTAX III REVOLUTION Trial has been previously described.[5] The risk reclassification is presented as the proportion of patients reclassified from the anatomic to the functional SYNTAX score tertiles (ie, low <22, intermediate 23–32, and high >32). Comparison of the continuous anatomic SYNTAX scores was performed with the paired *t* test. Differences in categorical variables were assessed with the use of McNemar test, since they were from a matched population. Agreement between (1) SYNTAX II recommendation strategies derived from angiography only versus that derived from angiography with CTA and FFR_{CT} and between (2) tertiles of anatomic SYNTAX score derived from different imaging strategies were assessed with the concordance coefficient of κ. A 2-sided *P* value of 0.05 or less was considered to indicate statistical significance. All statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

From June 29, 2016 to February 8, 2018, 223 patients with left main or 3-vessel CAD were enrolled in 6 centers from 5 European countries. Baseline clinical characteristics and CT acquisition information are shown in Table II in the Data Supplement. Coronary CTA assessment was feasible in 99% of the patients, and the FFR_{CT} analysis was available in 196 patients (88% of the entire study population; Figure 1). FFR_{CT} was available for 1030 F1
lesions and was positive (≤0.80) in 89% of them (mean FFR_{CT} value 0.64±13; Figure 2). F2

Impact of FFR_{CT} on the Treatment Decision Based on Coronary CTA

Using coronary CTA alone, 1108 stenoses (5.0±1.7 per patient) were detected. The mean anatomic SYNTAX score derived from coronary CTA was 33.9±13.0 (n=233 patients). The heart teams subtracted 205 lesions, assessed as nonfunctionally significant, for the functional SYNTAX score calculation. This led to a reduction of the noninvasive functional SYNTAX score (n=196) to 30.5±13.0 (*P* value <0.001 versus anatomic SYNTAX score). The inclusion of the physiology component led to a mean reduction of the SYNTAX score of 3.7 points. Table 1 shows the impact of the physiology T1
information on the SYNTAX score components.

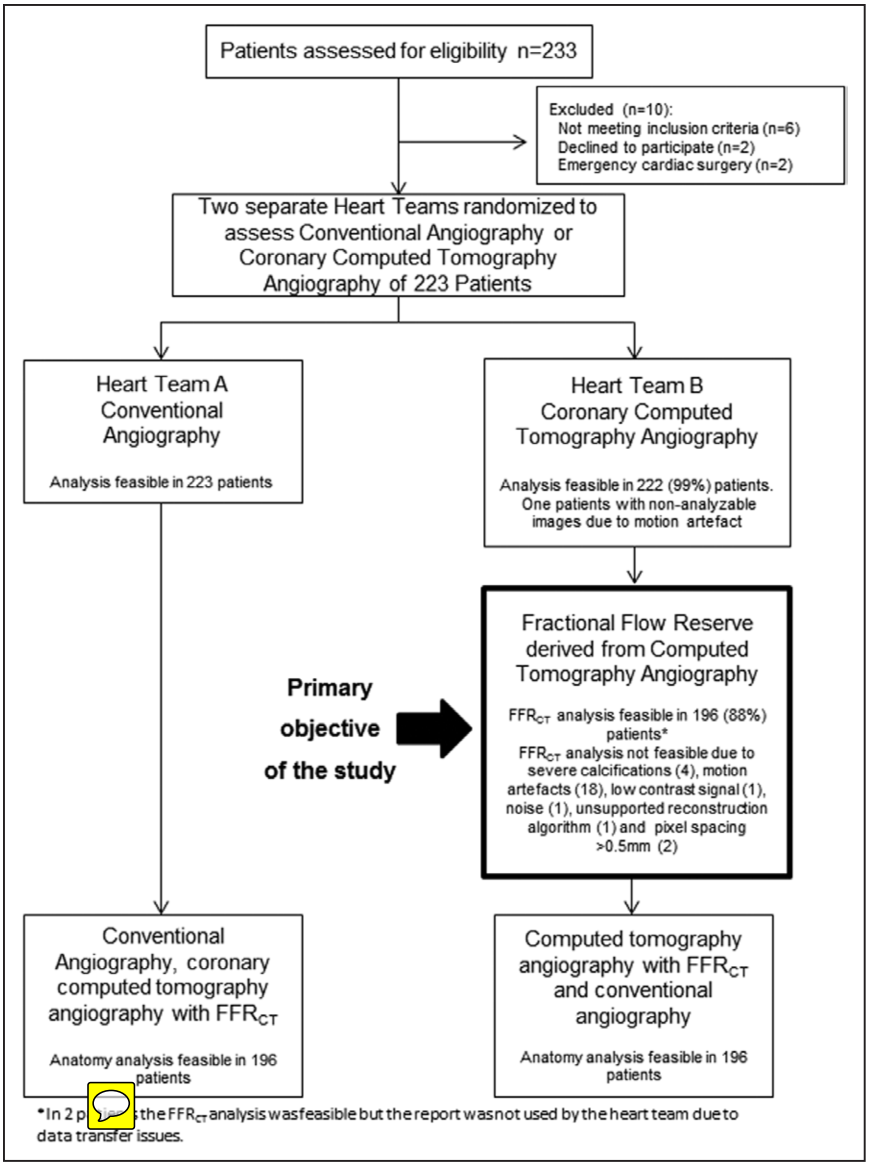

Figure 1. ~~**Revolution SYNTAX III Study flow chart.**~~ AQ15
FFR_{CT} indicates fractional flow reserve derived from computed tomography angiography.

Based on the functional SYNTAX score according to FFR_{CT}, SYNTAX score III recommended CABG only in 24% (47/194) of the patients and the heart team treatment decision was CABG in 69% (161/194) of the cases. FFR_{CT} changed the treatment decision between CABG and PCI in 7% (14/194) of the patients and modified the revascularization strategy in 12.1% of the vessels. Compared with anatomic coronary CTA assessment, addition of FFR_{CT} reduced the number of patients with significant 3-vessel CAD from 92.3% to 78.8%.

Impact of Coronary CTA With FFR_{CT} on Treatment Decision Based on Conventional Angiography

Conventional coronary angiography identified 1073 stenoses (4.8±1.7 per patient) with a mean SYNTAX score of 30.3±12.2. Further evaluation with coronary CTA and FFR_{CT} removed 129 nonhemodynamically significant lesions from the functional SYNTAX score calculation; however, the mean SYNTAX score remained unchanged (31.2±13.4; Table 2). The SYNTAX score III recommended CABG only in 26% (50/196) of the patients, and CABG was selected as the treatment by the heart team in 69% (135/196) of the patients. The addition of FFR_{CT} changed the heart team's treatment selection in 6.6% of patients and modified treatment planning in 18.3%. The number of patients with significant 3-vessel CAD remained unchanged (86.1% versus 86.2%). T2

Risk Reclassification

Using FFR_{CT}, 15.5% (30/194) of the patients were reclassified to a lower risk SYNTAX score tertile based on coronary CTA alone (Table III in the Data Supplement, Figure 3A). Similarly, the addition of noninvasive functional assessment to conventional angiography reclassified 14% (31/221) of the patients to a lower risk tertile F3

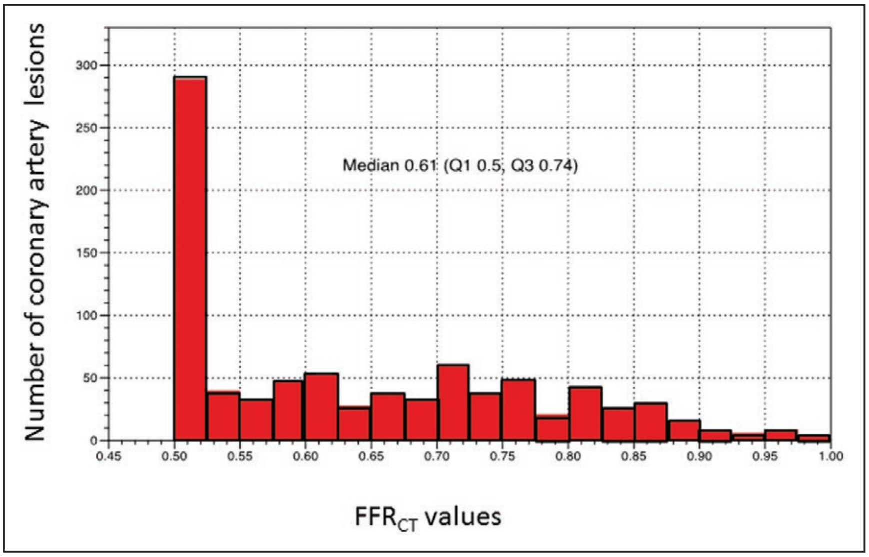

Figure 2. Flow reserve derived from computed tomography angiography (FFR_{CT}) values distribution. The diagram shows the number of lesions divided into incremental FFR_{CT} values. *Because the lower limit of detection of FFR_{CT} is 0.5, values presented at this interval 0.50–0.525 also represent all values below 0.5.

(Table IV in the Data Supplement, Figure 3B). The recommendation based on the SYNTAX II score changed in 6.7% of the patients (ie, in 3.1% of the patients, the recommendation changed from CABG only to equipoise by adding FFR_{CT} to conventional angiography, and in 3.6% the recommendation changed from equipoise to CABG only). The agreement was high with a κ of 0.82
T3 (0.73–0.92; Table 3).

DISCUSSION

The main findings of the present study can be summarized as follows: (1) by including the noninvasive functional evaluation with FFR_{CT}, the heart team changed the treatment recommendation in 7% of the cases and modified the selection of vessels for revascularization in 12% as compared with a coronary CTA assessment alone. Moreover, inclusion of FFR_{CT} information on top of conventional angiography changed the treatment recommendation in 6.6% of the cases and modified the planning in 18.3%; (2) the noninvasive functional SYNTAX score reclassified 15.5% of the patients to a lower SYNTAX score tertile based on coronary CTA and 14% of the patients to a lower SYNTAX score tertile based on conventional angiography; and (3) in patients assessed by coronary CTA, FFR_{CT} reduced the proportion of patients with hemodynamically significant 3-vessel CAD from 92.3% to 78.8%.

It is noteworthy that in this study anatomically nonsignificant lesions were not scored in the calculation of the coronary CTA SYNTAX score, even if the FFR_{CT} in the distal vessel was positive. On the contrary, when FFR_{CT} was ≤0.8 in the proximal coronary segments, all distal lesions were considered significant. This approach might underestimate the clinical impact of FFR_{CT}, and technical improvements are ongoing to overcome the limitation.

Use of physiology-guided percutaneous revascularization has shown to reduce the rate of major adverse cardiovascular events compared with angiographic guidance alone and has been recommended by the latest guidelines to identify hemodynamically relevant lesions.[9] In the SYNTAX II study, which included patients with 3-vessel disease without left main involvement and moderate anatomic complexity (mean SYNTAX score 20.3±6.4), routine physicological assessment (performed in 82.8% of patients) reduced the percentage of patients with 3-vessel disease to 37.2%.[10] At variance with SYNTAX II, the SYNTAX III REVOLUTION trial included patients with more severe CAD, as underlined by a mean anatomic SYNTAX score of 30.0±12.0.[6] Moreover, the proportion of lesions with a positive FFR was 89% in SYNTAX III and 74.6% in SYNTAX II. In SYNTAX II, inclusion of FFR_{CT} reclassified 30% of the patients to a lower SYNTAX score tertile, which is a higher proportion than that observed in the present study. The limited exclusion criteria of SYNTAX III, particularly the inclusion of patients with left main coronary artery stenosis, are likely responsible for this finding and underline the functional compromise of unselected patients with multivessel CAD. Of note, 11% of the coronary lesions in this complex population were found to have a value higher than 0.80 at FFR_{CT}, and this finding influenced the treatment decision in 6% of the patients and modified treatment planning in 16%.

In a large, retrospective study, FFR-guided CABG is associated with a reduction in death and myocardial infarction compared with angiography-guided CABG at 6-year follow-up.[11] We may expect an increase in functional-guided CABG in the upcoming years. In particular, coronary CTA with FFR_{CT} may provide to interventional cardiologists and cardiac surgeons a combined anatomic and functional noninvasive assessment of multivessel disease for the type and modality of revascularization. Indeed, one of the potential advantages of FFR_{CT} is the possibility to interrogate the physiology of any segment in the epicardial coronary circulation.[12–14] From the heart

Table 1. Anatomy and Functional SYNTAX Score Assessment in the Heart Team Randomized to Coronary CTA

Characteristics	Coronary CTA Only 223 Patients	Coronary CTA With FFR_{CT} 194 Patients	*P* Value
Number of lesions	1108	903	
Diseased vessels			
RCA	95.5% (212/222)	86.6% (168/194)	<0.001
LAD	99.5% (221/222)	96.9% (188/194)	0.063
LCX	95.0% (211/222)	90.7% (176/194)	0.039
Left main	36.0% (80/222)	30.4% (59/194)	0.006
Anatomy and functional SYNTAX score components			
Total occlusion	12.0% (133/1108)	12.8% (116/903)	0.5
Trifurcation	2.2% (24/1108)	1.6% (14/903)	1.0
Bifurcation	23.4% (259/1108)	22.5% (203/903)	1.0
Type of bifurcation			
Medina 1,0,0	1.1% (12/1108)	1.1% (10/903)	1.0
Medina 0,1,0	0.8% (9/1108)	0.9% (8/903)	1.0
Medina 1,1,0	6.9% (77/1108)	6.9% (62/903)	1.0
Medina 1,1,1	8.6% (95/1108)	8.4% (76/903)	1.0
Medina 0,0,1	1.8% (20/1108)	1.6% (14/903)	1.0
Medina 1,0,1	1.9% (21/1108)	1.8% (16/903)	1.0
Medina 0,1,1	2.3% (25/1108)	1.9% (17/903)	1.0
Aorto-ostial lesion	3.6% (40/1108)	3.0% (27/903)	0.13
Severe tortuosity	0.9% (10/1108)	1.1% (10/903)	1.0
Length >20 mm	30.4% (296/975)	30.0% (236/787)	0.25
Heavy calcification	28.9% (320/1108)	27.1% (245/903)	1.0
Thrombus	0.3% (3/1108)	0.3% (3/903)	1.0
Anatomy and functional SYNTAX score	33.9±13.0	30.5±13.0	
1-vessel disease	0.9% (2/222)	3.1% (6/194)	0.22
2-vessel disease	6.8% (15/222)	18.0% (35/194)	<0.001
3-vessel disease	91.9% (204/222)	78.4% (152/194)	<0.001
Left main only	0.5% (1/222)	0.5% (1/194)	1.0
3-vessel disease (or 3-VD equivalent)	92.3% (204/221)	78.8% (152/193)	<0.001

McNemar test used to compare matched categorical variables. CTA indicates computed tomography angiography; FFR_{CT}, fractional flow reserve derived from computed tomography angiography; LAD, left anterior artery; LCX, left circumflex; and RCA, right coronary artery.

team's perspective, a nonhemodynamically significant lesion in the left anterior descending artery may prompt a change in the treatment strategy, favoring a percutaneous interventional approach in a multivessel disease patient. Moreover, in patients undergoing CABG, the recognition of nonhemodynamically significant lesions may reduce unnecessary grafts, surgical time, and might result in higher graft patency. The ongoing FAME 3 Trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation), a comparison of FFR-guided PCI and CABG surgery in patients with multivessel CAD, will provide further clinical evidence of the potential benefit of FFR-guided surgical revascularization.[15]

Table 2. Anatomy and Functional SYNTAX Score Assessment in The Heart Team Randomized to Conventional Angiography

Characteristics	Conventional Angiography First Strategy		*P* Value
	Conventional Angiography Only 223 Patients	Conventional Angiography and Coronary CTA With FFRCT 196 Patients	
Number of lesions	1073	944	
Diseased vessels			
RCA	92.4% (206/223)	93.9% (184/196)	1.0
LAD	96.4% (215/223)	97.4% (191/196)	0.63
LCX	95.1% (212/223)	92.3% (181/196)	0.15
Left main diseased	28.7% (64/223)	28.1% (55/196)	1.0
Anatomy and functional SYNTAX score components:			
Total occlusion	14.0% (150/1073)	13.6% (128/944)	0.42
Trifurcation	2.4% (26/1073)	2.2% (21/944)	1.0
Bifurcation	22.0% (236/1073)	21.3% (201/944)	0.88
Type of bifurcation			
Medina 1,0,0	1.7% (18/1073)	1.2% (11/944)	0.07
Medina 0,1,0	2.6% (28/1073)	1.8% (17/944)	0.33
Medina 1,1,0	4.4% (47/1073)	5.0% (47/944)	0.28
Medina 1,1,1	6.8% (73/1073)	7.2% (68/944)	0.66
Medina 0,0,1	2.4% (26/1073)	1.5% (14/944)	0.21
Medina 1,0,1	2.2% (24/1073)	2.8% (26/944)	0.23
Medina 0,1,1	1.9% (20/1073)	1.9% (18/944)	0.84
Aorto-ostial lesion	3.3% (35/1073)	3.7% (35/944)	0.86
Severe tortuosity	2.2% (24/1073)	0.8% (8/944)	0.002
Length >20 mm	29.1% (269/923)	30.1% (246/816)	0.15
Heavy calcification	13.0% (140/1073)	20.9% (197/944)	<0.001
Thrombus	0.3% (3/1073)	0.6% (6/944)	0.125
Anatomy and functional SYNTAX score	30.3±12.2	31.2±13.4	
1-vessel disease	1.3% (3/223)	1.5% (3/196)	1.0
2-vessel disease	12.1% (27/223)	11.7% (23/196)	1.0
3-vessel disease	86.1% (192/223)	86.2% (169/196)	0.82
Left main only	0.4% (1/223)	0.5% (1/196)	1.0
3-vessel disease (or 3-VD equivalent)	86.5% (192/222)	86.7% (169/195)	0.82

McNemar test used to compare matched categorical variables. CTA indicates computed tomography angiography; FFR_{CT}, fractional flow reserve derived from computed tomography angiography; LAD, left anterior artery; LCX, left circumflex; and RCA, right coronary artery.

Practical implementation of pressure-wire assessment of coronary lesions is still low worldwide. Furthermore, multivessel FFR or instantaneous wave-free ratio evaluation is seldom performed before a revascularization procedure, particularly before CABG. FFR_{CT} has the potential to refine the heart team's treatment decision and planning by incorporating the functional component of coronary epicardial lesions. The results of the present study support the feasibility and utility of preprocedural physiology assessment to better select and guide the

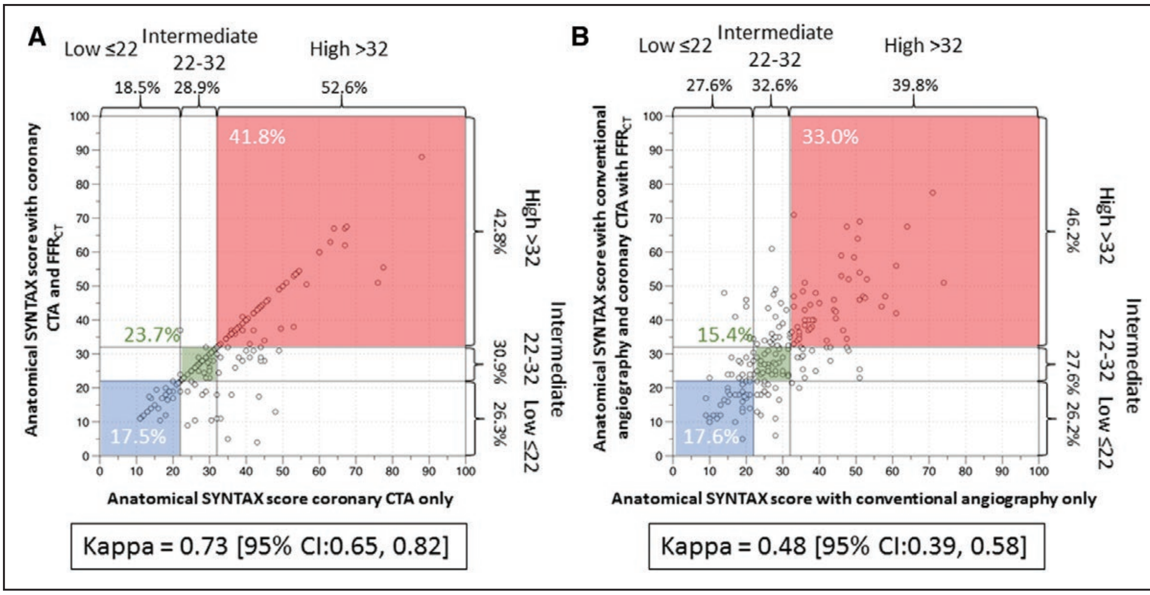

Figure 3. Flow reserve derived from computed tomography angiography (FFR_{CT}) and risk reclassification.
AQ7 The figure shows the impact of the noninvasive functional SYNTAX score on risk reclassification of patients assessed by coronary computed
AQ8 tomography angiography (CTA; **A**) and [illegible] **B**). The red, green, and blue squares show the proportion of patients in whom the 2 imaging techniques are concordant in SYNTAX risk classification, respectively.

revascularization strategy in patients with multivessel CAD. Moreover, the high accuracy of FFR_{CT} in patients with multivessel disease and the safety regarding radiation dose achievable with the latest generation scanners[16] make the noninvasive physiology assessment a very promising tool for the evaluation of patients with multivessel disease before a revascularization procedure. Progress in the field of coronary CTA, FFR_{CT}, and the application of machine learning on fluid dynamic analysis have proven to be clinically relevant.[17] Of note, the acceptance rate for FFR_{CT} analysis in the present study was very high (88%), particularly if compared with that reported in other prospective multicenter trials. For example, it was 33% in the PROMISE trial[18] and 69% in the SYNTAX II.[4] However, the high rate of coronary CTA suitability for FFR_{CT} appears not surprising if we consider the scanner used in the SYNTAX III trial that combines fast gantry rotation time and intracycle motion-correction algorithm aimed at reducing the impact of motion artifacts on image quality.[19]

Table 3. Level of Agreement Between Conventional Angiography Only vs Coronary CTA and Conventional Angiography With Functional Assessment by FFR_{CT}

Recommendation Based on Angiography Only	Recommendation Based on Angiography and Coronary CTA With FFRCT		
	CABG Only		PCI Only/Equipoise
CABG only	21.9% (43/196)		3.1% (6/196)
PCI only/equipoise	3.6% (7/196)		71.4% (140/196)
	Number	%, 95% CI	κ, 95% CI
Concordance	183	93.4 (88.9–96.4)	0.82 (0.73–0.92)

Recommendation are based on SYNTAX II Score. CABG indicates coronary artery bypass grafting; CTA, computed tomography angiography; FFR_{CT}, fractional flow reserve derived from computed tomography angiography; and PCI, percutaneous coronary ~~intervent~~[illegible]

Future Perspectives

The present study opens new perspectives on the use of coronary CTA as a tool to provide the interventionalist and cardiac surgeon with an anatomy and functional noninvasive road-map for myocardial revascularization strategy. Moreover, full automation of the SYNTAX III score has the potential to further enhance the decision-making process in patients with multivessel disease. The interactive planner, which is a new application of FFR_{CT}, could improve treatment selection while tailoring procedural planning based on assessing functional outcomes after virtual treatment.[20] In this novel and growing clinical field, stress myocardial CT perfusion has been introduced as a new tool for evaluating the functional relevance of coronary stenoses.[21–25] However, unlike FFR_{CT}, CT perfusion requires an additional scan, use of a stressor agent, and is associated with higher radiation exposure.[26] Moreover, use of an adenosine-stress protocol may raise some safety concerns particularly in patients with left main or 3-vessel CAD.

Limitations

Some limitations of this study should be acknowledged. First, due to the study design, no data on the diagnostic accuracy of FFR_{CT} versus invasive FFR were assessed. However, physiological evaluation with FFR_{CT} has been shown to be accurate in multivessel CAD patients.[4] Second, SYNTAX III Revolution was a decision-making trial;

thus, the clinical application of FFR_{CT} derived SYNTAX III score requires further investigation in a clinical outcome trial. Third, we recognize that this study was not designed to indicate to what degree FFR_{CT} may influence patients management.

Conclusions

In patients with left main or 3-vessel CAD, a noninvasive physiology assessment using FFR_{CT} changed heart team's treatment decision-making and selection of vessels for revascularization in one-fifth of the patients. This may improve the appropriateness and clinical outcome of myocardial revascularization treatment.

ARTICLE INFORMATION

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