Radiology: Cardiothoracic Imaging

SPECIAL REPORT

Selective Use of CT Fractional Flow at a Large Academic Medical Center: Insights from Clinical Implementation after 1 Year of Practice

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Purpose: This special report outlines a retrospective observational study of CT fractional flow reserve (CT-FFR) analysis using dual-source coronary CT angiography (CTA) scans performed without heart rate control and its impact on clinical outcomes.

Materials and Methods: All patients who underwent clinically indicated coronary CTA between August 2020 and August 2021 were included in this retrospective observational study. Scans were performed in the late systolic to early diastolic period without heart rate control and analyzed at the interpreting physician's discretion. Demographics, coronary CTA features, and rates of invasive coronary angiography (ICA), percutaneous coronary intervention (PCI), myocardial infarction, and all-cause death at 3 months were assessed by chart review.

Results: During the study period, 3098 patients underwent coronary CTA, of whom 113 with coronary bypass grafting were excluded. Of the remaining 2985 patients, 292 (9.7%) were referred for CT-FFR analysis. Two studies (0.7%) were rejected from CT-FFR analysis, and six (2.1%) analyses did not evaluate the lesion of concern. A total of 160 patients (56.3%) had CT-FFR greater than 0.80. Among patients with significant stenosis at coronary CTA, patients who underwent CT-FFR analysis presented with lower rates of ICA (74.5% vs 25.5%, P = .04) and PCI (78.9% vs 21.1%, P = .05).

Conclusion: CT-FFR was implemented in patients not requiring heart rate control by using dual-source coronary CTA acquisition and showed the potential to decrease rates of ICA and PCI without compromising safety in patients with significant stenosis and an average heart rate of 65 beats per minute.

Supplemental material is available for this article.

The primary goal of coronary CT angiography (CTA) is to identify coronary artery disease. However, not all coronary stenoses are hemodynamically significant, despite their anatomic appearance.

Obstructive coronary artery disease identified with noninvasive imaging warrants medical treatment, and revascularization is the preferred strategy for those with persistent symptoms (1,2).

Identifying functionally significant obstructions can help safely defer further invasive coronary angiography (ICA) and revascularization. Traditionally, this has hinged on invasive physiologic measurements such as fractional flow reserve (1,2). However, noninvasive modalities such as CT fractional flow reserve (CT-FFR) are now approved for clinical use in the United States. The addition of CT-FFR to CTA has demonstrated significant improvements in pooled specificities when compared with CTA alone (3), which has shown a high negative predictive value but relatively weak specificity in most previously published research (4,5). Furthermore, CT-FFR results have previously been found to appropriately change management in most cases initially planned for revascularization to medical management (6).

The rates of technically unsuccessful CT-FFR were found to be 2.9% in the ADVANCE registry (7). However, it was observed that a lower patient heart rate may lead to an increase in the rates of successful completion of CT-FFR analysis (8). The quality of CTA images is largely dependent on the patient's heart rate during the scan, with lower rates often yielding superior results. According to the Society of Cardiovascular Computed Tomography, scanning at higher heart rates can introduce complications, such as motion artifacts and suboptimal contrast enhancement (9). While heart rate control can enhance image quality at CTA, it comes with potential drawbacks, including adverse effects from medications, contraindications for certain patients, procedural delays, risks of rebound tachycardia, patient noncompliance, and additional costs.

Abbreviations

CAD-RADS = Coronary Artery Disease Reporting and Data System, CTA = CT angiography, CT-FFR = CT fractional flow reserve, ECG = electrocardiography, ED = emergency department, ICA = invasive coronary angiography, PCI = percutaneous coronary intervention

Summary

CT fractional flow reserve analysis of dual-source CT scans performed without heart rate control in patients with significant stenosis resulted in a lower frequency of invasive coronary angiography and percutaneous coronary intervention, without compromising safety.

Keywords

Angiography, CT, CT-Angiography, Fractional Flow Reserve, Cardiac, Heart, Arteriosclerosis

We recently implemented CT-FFR into our high-volume clinical service and conducted a retrospective observational study to assess the feasibility of CT-FFR analysis using dual-source CT scans performed without using β-blockers and its impact on clinical outcomes. These observations may be helpful for other clinical services seeking to incorporate CT-FFR into practice.

Materials and Methods

Study Design and Patient Selection

This retrospective study was performed under an institutional review board–approved and Health Insurance Portability and Accountability Act–compliant protocol. The requirement for informed consent was waived. The study was not sponsored or initiated by the vendor (who was not involved in the study design or this manuscript), and the authors had complete control of all data.

All patients who underwent clinically indicated coronary CTA between August 11, 2020, and August 11, 2021, were included. At the interpreting physician's discretion, patients with mild to severe coronary stenoses (reported according to the Coronary Artery Disease Reporting and Data System [CAD-RADS] [10]) of possible hemodynamic significance could be selected for CT-FFR analysis (HeartFlow). Clinical judgment was the key factor in determining which patients were selected for this analysis.

Coronary CTA Acquisition

Scans were performed using a second- or third-generation dual-source CT scanner (SOMATOM Definition Flash or SOMATOM Force; Siemens Healthineers) using electrocardiography (ECG) synchronization by a qualified technologist, with monitoring of all examinations by a subspecialty radiologist or cardiologist. Prospectively ECG-triggered noncontrast scans were performed in all patients for calcium scoring before contrast-enhanced scans but were not used to make triage, cancellation, or scan parameter decisions. Prospectively ECG-triggered axial-sequential acquisition with arrhythmia rejection (Adaptive Cardio Sequential; Siemens) was used preferably over retrospective ECG-triggered acquisition, as per standard service protocol for CTA (11). CTA tube current and potential were automatically optimized (CAREkV and CAREDose 4D; Siemens Healthineers). Breast displacement was performed as applicable (12). Scan acquisitions were performed during a single breath hold at end inspiration, with the z-axis scan ranging from the level of the carina to the diaphragm. Bolus triggering was used for contrast timing. All patients included in the study underwent coronary CTA without heart rate control, regardless of their baseline heart rate. During scanning, all heart rates and rhythms were accepted for scanning, provided patients were hemodynamically stable. Unless contraindicated, transdermal or sublingual nitroglycerin was administered during the examination. All examinations were checked for notable artifacts by a qualified interpreting physician before patient dismissal from the examination table, to ensure high image quality (as per standard practice) (13,14). Maroules et al (15) have previously published data regarding the protocols Ghoshhajra et al (16) followed in the cardiac CT service, using the 200–400-msec interval.

CT-FFR Analysis

Under supervision from a cardiovascular imaging staff member with more than 10 years of postsubspecialty fellowship experience (B.B.G.), three clinical professionals (P.G.R., E.Z., A.P.) and two research cardiovascular imaging fellows (V.T., A.K.T.), all of whom are trained in the use of CT-FFR and have 3, 3, 9, and 2 years of experience in cardiovascular imaging research, respectively, analyzed CT-FFR and coronary CTA results at the patient and vessel level. They graded lesions involving coronary segments greater than 1.5 mm in lumen diameter according to the clinically reported stenosis per the CAD-RADS scoring system. In our study, we followed guidelines that recommend measuring the lowest CT-FFR value within 2 cm distal to the lesion of concern (17). We did not include false-positive values from low terminal vessels with a diameter of less than 1.5 mm in our analysis. CT-FFR values were categorized into three groups: CT-FFR greater than 0.80 indicates insignificant hemodynamic significance, CT-FFR less than or equal to 0.75 suggests high hemodynamic significance, and CT-FFR greater than 0.75 and less than or equal to 0.80 represents an intermediate category with uncertain significance, requiring additional risk stratification for appropriate decisions (18). These categories aid in determining the need for invasive procedures and optimizing treatment strategies based on disease severity.

Other collected data included coronary calcium scores (a part of the standard CTA protocol in all cases), the presence of coronary plaque, heart rate during the scan, and radiation doses. These data on plaque categorization, in addition to the calcium score, were included to account for both calcified and noncalcified plaques. Additionally, an in-depth analysis of the correlation between CTA and ICA, for anatomic stenoses, was performed. The readers assessed ICA, percutaneous coronary intervention (PCI), myocardial infarction, and death at 3 months using codes existing in the patient charts. This relatively shorter follow-up duration was selected to include the maximum number of

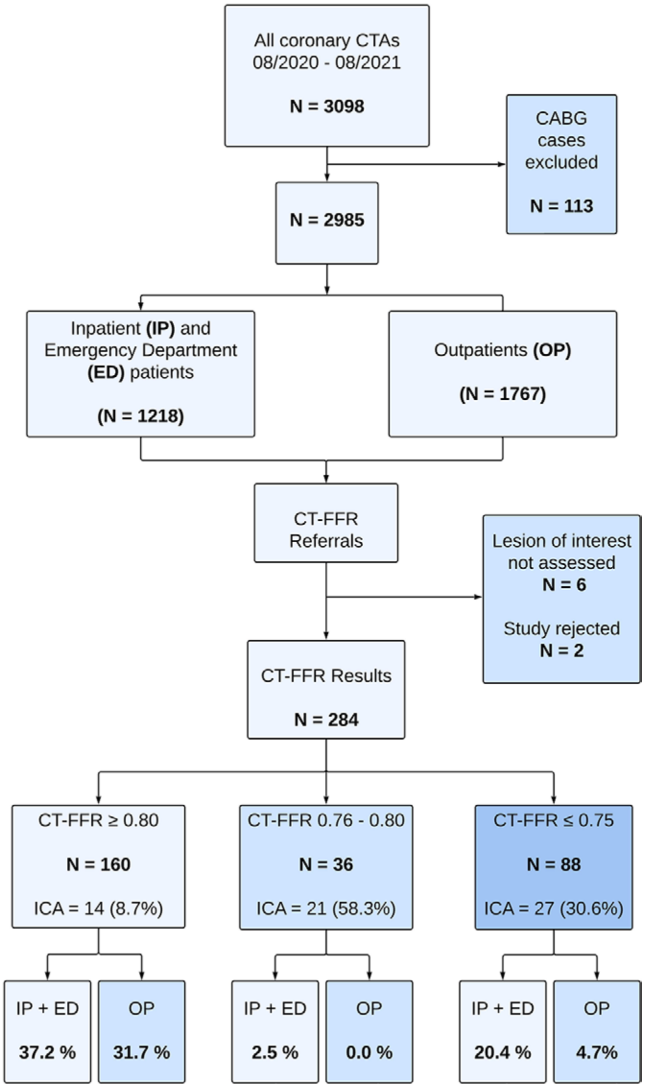

Figure 1: Study flow diagram. CABG = coronary artery bypass grafting, CTA = CT angiography, CT-FFR = CT fractional flow reserve, ED = emergency department, ICA = invasive coronary angiography, IP = inpatient, OP = outpatient.

patients possible, as most patients would have undergone least a 3-month follow-up.

Statistical Analysis

We compared the patients who did and did not undergo CT-FFR analysis and analyzed the three categories based on CT-FFR results of 0.75 or less, 0.76–0.80, and greater than 0.80.

Results are presented as counts and percentages, means and SDs, or medians and IQRs, as appropriate. Student *t* test or nonparametric Mann-Whitney tests were used for continuous group comparisons, while a χ^2 test, Fisher exact test, or a sign test were used for categorical comparisons. Logistic regression was utilized to adjust for confounders (age, sex, comorbidities, and severity of coronary lesions) and assess the association between CT-FFR analysis and patient outcomes. All tests were two-tailed with an α level of .05. Calculations were performed in Python SciPy (version 1.7.3) by two of the authors (A.K.T., M.K.R.).

Results

Study Population and Referral Patterns

During the study period, 3098 patients underwent coronary CTA, of whom 113 patients with coronary bypass grafting were excluded. The most common cause of CTA referral was angina or anginal equivalent. Of the 2985 patients, 292 (9.7%) were referred for CT-FFR (Fig 1).

Most of the patients included in the CT-FFR and non–CT-FFR groups were outpatients (1767 of 2985), as seen in Figure S1. During the study, only two cases (0.7%) were rejected from CT-FFR analysis, and six (2.1%) analyses did not evaluate the lesion of concern because of small vessel caliber. Of these six cases, all were discussed for possible re-evaluation and escalated when relevant and possible clinically under the knowledge and guidance of the clinical division chief.

Patient Demographics and Baseline Characteristics

Overall patient characteristics are shown in Table 1, and scan parameters are mentioned in Table 2. Other scan and patient characteristics from our CT service, including scan parameters according to body mass index classes and sex, have been published previously (12,15). Patients selected for CT-FFR analysis were older, more often male, and had a higher prevalence of hypertension, hyperlipidemia, coronary calcium, and coronary plaque than those who did not undergo CT-FFR.

In our study, we found that 1700 of the 2985 total patients (57.0%) were not using any heart rate–lowering medications, with a mean heart rate of 66.2 beats per minute. On the other hand, 1285 patients (43.0%) were taking at least one heart rate–lowering medication and had a lower mean heart rate of 61.8 beats per minute.

CT-FFR Analysis and Anatomic Stenosis

The majority of the 284 evaluable CT-FFR examinations fell into CAD-RADS category 3 or higher (corresponding to moderate to severe anatomic stenoses), of which 209 (73.6%) were CAD-RADS 3 lesions (Fig 2A). CT-FFR was not requested by the interpreting physician in 58 patients with CAD-RADS 3, among whom 11 had extensive coronary calcium (Agatston score > 1000, although this is not a contraindication to CT or CT-FFR) and eight had stents, which hindered CT-FFR analysis. Conversely, only 65 of 294 (22.1%) scans with CAD-RADS grade above 3 were sent for CT-FFR analysis. Most of these patients (41 of 65, 63.1%) proceeded directly to ICA because of extensive calcification, presence of stents, or prior bypass grafts.

Of the 284 patients with evaluable CT-FFR results, 160 (56.3%) had CT-FFR greater than 0.80 and 88 (30.9%) had CT-FFR less than or equal to 0.75, while the remaining 36 patients (12.6%) had borderline CT-FFR results between 0.76 and 0.80. Anatomic severity was associated with higher positive (<0.80) CT-FFR rates. The rates of hemodynamically significant disease grouped by examination location and their outcomes are shown in Figure 2. At the per-vessel level, 1135 epicardial arteries were assessed. Lesions in the left anterior descending coronary

Table 1: Characteristics of Patients with and without CT-FFR Analysis and Examination Location

					IP + ED (*n* = 1218)			OP (*n* = 1767)		
Characteristic	Total	Without CT-FFR	With CT-FFR	*P* Value	Without CT-FFR	With CT-FFR	*P* Value	Without CT-FFR	With CT-FFR	*P* Value
No. of patients	2985	2693	284		1043	171		1650	113	
Age (y)	60.0 (50.0–69.0)	59.0 (50.0–69.0)	66.0 (60.0–74.0)	<.001	56.8 (47.0–67.0)	66.9 (61.0–75.0)	<.001	59.2 (51.0–70.0)	66.1 (60.0–73.0)	<.001
Male sex	1682/2985 (56.3)	1491/2693 (55.3)	191/284 (67.2)	<.001	596/1043 (57.1)	81/171 (47.3)	.66	895/1650 (54.2)	110/113 (97.3)	<.001
BMI	28.2 ± 4.7	28.4 ± 4.9	29.8 ± 5.1	.02	29.1 ± 4.9	29.4 ± 4.1	.88	28.1 ± 4.4	28.1 ± 4.9	.95
Heart rate–lowering medication use	1285/2985 (43.0)	1145/2693 (38.3)	140/284 (4.6)	.14	509/1043 (48.8)	48/171 (28.0)	<.001	636/1650 (38.5)	92/113 (81.4)	.02
Hypertension	1498/2985 (50.1)	1318/2693 (48.9)	180/284 (63.4)	<.001	669/1043 (64.1)	74/171 (43.2)	<.001	649/1650 (39.3)	106/113 (93.8)	<.001
Hyperlipidemia	1254/2985 (42.0)	1084/2693 (40.2)	170/284 (59.9)	<.001	566/1043 (54.2)	77/171 (45.0)	<.001	518/1650 (31.3)	93/113 (82.3)	<.001
Diabetes	469/2985 (15.7)	416/2693 (15.4)	53/284 (18.7)	.26	192/1043 (18.4)	17/171 (9.9)	.78	224/1650 (13.5)	36/113 (31.8)	.10
Chronic kidney disease	208/2985 (6.9)	191/2693 (7.0)	17/284 (6.0)	.52	72/1043 (6.9)	9/171 (5.2)	.80	119/1650 (7.2)	8/113 (7.0)	.56
Tobacco use	738/2985 (24.7)	657/2693 (24.3)	81/284 (28.5)	.23	271/1043 (25.9)	27/171 (15.7)	.68	386/1650 (23.3)	54/113 (47.7)	.07
Obesity	461/2985 (15.4)	419/2693 (15.5)	42/284 (14.8)	.89	157/1043 (15.0)	20/171 (11.7)	.16	262/1650 (15.8)	22/113 (19.4)	.34
Stent*	369/2985 (12.3)	365/2693 (13.5)	4/284 (1.4)	<.001	148/1043 (14.1)	0/171 (0)	.001	217/1650 (13.1)	4/113 (3.5)	<.001

Note.—Continuous data are presented as medians, with IQRs in parentheses, or means ± SDs, and categorical data are presented as counts, with percentages in parentheses. Of the patients referred to CT-FFR analysis, two studies were rejected and six analyses did not evaluate the lesion of concern. *P* values are comparing those with and without CT-FFR. BMI = body mass index, calculated as weight in kilograms divided by height in meters squared, CKD = chronic kidney disease, CT-FFR = CT fractional flow reserve, ED = emergency department, IP = inpatient, OP = outpatient.
* CT-FFR performed in native vessel without a stent.

artery had a higher degree of stenosis than those in the left main coronary artery, left circumflex coronary artery, and right coronary artery ($P < .001$).

Clinical Outcomes and Follow-up

The study patients were followed up for 3 months to detect any unfavorable adverse events, including mortality from any cause or myocardial infarction, as well as any interventions such as ICA and PCI. Analyses performed to highlight the differences between inpatient and emergency department (ED) and outpatient cohorts showed that significant stenoses were found in 331 of 1218 patients (27.2%) in the inpatient and ED cohort and 406 of 1767 patients (23.0%) in the outpatient cohort. Among patients with significant stenosis at coronary CTA (CAD-RADS 3 or above), patients who underwent CT-FFR analysis presented lower rates of ICA (74.5% vs 25.5%, $P = .04$) and PCI (78.9% vs 21.1%, $P = .05$) compared with those who did not undergo CT-FFR. In the CT-FFR group, of the 62 (22.7%) patients referred for ICA, 12 (19.4%) were found to have 50% or greater stenosis, 14 (22.6%) had a stenosis 70% or greater, and 11 (17.7%) had a stenosis of 90% or greater at invasive angiography (Table 3). Outcomes of patients with significant stenosis are mentioned in Tables S1 and S2. Thirty-eight of 2693 (1.41%) patients in the non–CT-FFR group and four of 292 (1.36%) from the CT-FFR group had nondiagnostic image quality (Table 4).

Of a total of 36 deaths overall, metastatic cancer (seven, 19.4%) was the most common cause of mortality, followed by end-stage liver disease (five, 13.8%) and heart failure (four, 11.1%) (Fig S2).

Image Quality and Diagnostic Concordance

The correlation between anatomic stenoses seen at CTA and ICA in patients with and without CT-FFR analysis is shown in Figure 3. We observed 100% concordance in the CT-FFR group and a discordance rate of 2.2% in the non–CT-FFR group, using the threshold of a difference of 30% or greater to define discordance (Cohen weighted κ = 0.72).

Table 2: Cardiac CT Characteristics of Patients with and without CT-FFR Analysis and Examination Location

					IP + ED (*n* = 1218)			OP (*n* = 1767)		
Characteristic	Total	Without CT-FFR	With CT-FFR	*P* Value	Without CT-FFR	With CT-FFR	*P* Value	Without CT-FFR	With CT-FFR	*P* Value
No. of patients	2985	2693	284		1043	171		1650	113	
Heart rate (beats/min)	65.0 (57.0–76.0)	65.0 (57.0–76.0)	63.0 (55.0–76.0)	.09	71.2 (60.0–81.0)	71.1 (57.5–83.0)	0.89	67.5 (60.5–78.0)	64.0 (52.7–72.0)	.17
DLP (mSv)	4.4 (2.6–8.8)	4.4 (2.6–8.9)	4.8 (2.9–8.3)	.29	4.6 (2.0–8.3)	4.8 (2.2–8.6)	0.07	4.7 (2.4–8.2)	4.3 (2.0–7.2)	.08
Plaque location										
LM	889/2985 (29.8)	717/2693 (26.6)	172/284 (60.6)	<.001	717/1043 (68.7)	154/171 (90.0)	<0.001	0/1650 (0.0)	18/113 (15.9)	<.001
LAD	1767/2985 (59.1)	1502/2693 (55.7)	265/284 (93.3)	<.001	547/1043 (52.4)	157/171 (91.8)	<0.001	955/1650 (57.8)	108/113 (95.5)	<.001
LCx	1240/2985 (41.5)	1002/2693 (37.2)	238/284 (83.8)	<.001	308/1043 (29.5)	155/171 (90.5)	<0.001	694/1650 (42.0)	83/113 (73.4)	<.001
RCA	1470/2985 (49.2)	1211/2693 (44.9)	259/284 (91.2)	<.001	397/1043 (38.0)	159/171 (92.9)	<0.001	814/1650 (49.3)	100/113 (88.5)	<.001
Calcium score (HU)	14.5 (0.0–226.2)	6.0 (0.0–143.0)	453.0 (158.5–1089.0)	<.001	203.1 (0.0–101.0)	853.5 (153.0–1213.5)	<0.001	12.4 (0.0–769.0)	751 (159.7–1089.2)	<.001
CAD-RADS ≥ 3	711/2985 (23.8)	437/2693 (16.2)	274/284 (96.5)	<.001	140/1043 (13.4)	165/171 (96.4)	0.40	297/1650 (18.0)	109/113 (96.4)	.26
CAD-RADS score				<.001			<0.001			<.001
0	897/2985 (30.0)	897/2693 (33.3)	0/284 (0.0)		474/1043 (45.4)	0/171 (0.0)		423/1650 (25.6)	0/113 (0.0)	
1	537/2985 (17.9)	537/2693 (19.9)	0/284 (0.0)		196/1043 (18.8)	0/171 (0.0)		341/1650 (20.6)	0/113 (0.0)	
2	835/2985 (27.9)	825/2693 (30.6)	10/284 (3.5)		206/1043 (19.7)	3/171 (1.7)		619/1650 (37.5)	7/113 (6.1)	
3	278/2985 (9.3)	69/2693 (2.5)	209/284 (73.6)		0/1043 (0.0)	117/171 (68.4)		69/1650 (4.1)	92/113 (81.4)	
4A	289/2985 (9.6)	233/2693 (8.6)	56/284 (19.7)		91/1043 (8.7)	41/171 (23.9)		142/1650 (8.6)	15/113 (13.2)	
4B	82/2985 (2.7)	75/2693 (2.7)	7/284 (2.4)		25/1043 (2.4)	5/171 (2.9)		50/1650 (3.0)	2/113 (1.7)	
5	62/2985 (2.1)	60/2693 (2.2)	2/284 (0.7)		24/1043 (2.3)	2/171 (1.1)		36/1650 (2.1)	0/113 (0.0)	
Patients with significant stenosis	737/2985 (24.7)	463/2693 (17.2)	274/284 (96.4)	<.001	166/1043 (15.9)	165/171 (96.4)	<0.001	297/1650 (18.0)	109/113 (96.4)	<.001
ICA	243/2985 (8.1)	181/2693 (6.7)	62/284 (21.8)	.04*	112/1043 (10.7)	55/171 (32.1)	0.05*	69/1650 (4.1)	7/113 (6.1)	.08*
PCI	123/2985 (4.1)	97/2693 (3.6)	26/284 (9.1)	.05*	39/1043 (3.7)	19/171 (11.1)	0.87*	58/1650 (3.5)	7/113 (6.1)	.46*

Note.—Data are presented as medians, with IQRs in parentheses, or counts, with percentages in parentheses. CAD-RADS = Coronary Artery Disease Reporting and Data System, CKD = chronic kidney disease, CT-FFR = CT fractional flow reserve, DLP = dose-length product, ED = emergency department, ICA = invasive coronary angiography, IP = inpatient, LAD = left anterior descending artery, LCx = left circumflex artery, LM = left main artery, OP = outpatient, PCI = percutaneous coronary intervention, RCA = right coronary artery, SCAD = spontaneous coronary artery dissection.

* *P* value has been adjusted for confounders.

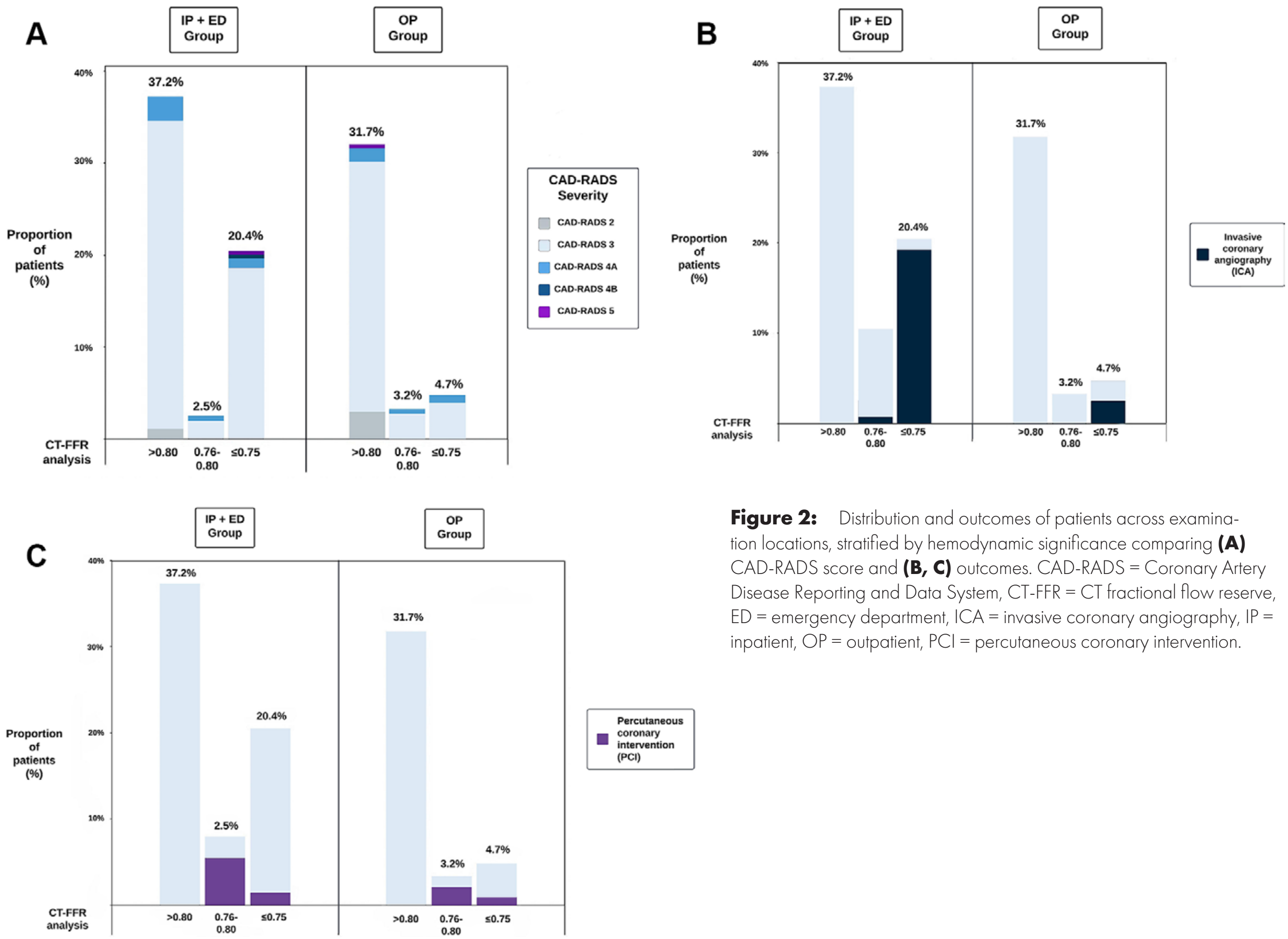

Figure 2: Distribution and outcomes of patients across examination locations, stratified by hemodynamic significance comparing **(A)** CAD-RADS score and **(B, C)** outcomes. CAD-RADS = Coronary Artery Disease Reporting and Data System, CT-FFR = CT fractional flow reserve, ED = emergency department, ICA = invasive coronary angiography, IP = inpatient, OP = outpatient, PCI = percutaneous coronary intervention.

Additional Study Metrics

There was no evidence of a difference in the median heart rates between both groups (63 beats per minute [IQR: 55–76] in the CT-FFR group vs 65 beats per minute [IQR: 57–76] in the non–CT-FFR group, $P = .10$, data available for the last 9 months). Among patients with CAD-RADS grade 3, the heart rates were also similar ($P = .92$). There was no evidence of a difference in radiation dose between the groups ($P = .29$).

Discussion

In summary, the key observations were as follows: *(a)* Using our standard protocols, the majority of the studies referred for CT-FFR were accepted for CT-FFR analysis, indicating the feasibility of performing CT-FFR without heart rate control, using dual-source coronary CTA acquisition; *(b)* CT-FFR was selectively performed in 9% of all coronary CTA procedures (the majority being moderate-grade stenoses), and results were negative for hemodynamically significant disease in 56.3%; and *(c)* among patients with significant stenosis at coronary CTA (CAD-RADS 3 or above), patients who underwent CT-FFR analysis presented lower rates of ICA and PCI without compromising safety.

An important aspect of our study revolves around the distinction between the inpatient and ED cohort and the outpatient cohort, with the following key differences observed between the two groups: *(a)* negative CT-FFR results (>0.80): more outpatients had CT-FFR results greater than 0.80, suggesting milder disease or fewer significant lesions in this group; *(b)* disease severity: inpatients and ED patients might present with more severe disease manifestations than outpatients; *(c)* resource utilization: outpatients, with a higher proportion of CT-FFR results greater than 0.80, may lead to less additional resource utilization, such as the need for ICA or other diagnostic procedures, compared to the inpatient and ED cohort.

Coronary CTA effectively assesses patients with new-onset stable chest pain and suspected coronary artery disease (19,20). Due to its high sensitivity, coronary CTA is recommended for imaging low- to intermediate-risk patients (21,22) but is less effective in identifying functionally significant coronary lesions (23,24). CT-FFR addresses this limitation without additional scans, procedures, or radiation exposure. As shown in the ADVANCE registry and the PLATFORM trial, CT-FFR has high diagnostic accuracy relative to ICA in detecting functionally significant coronary stenoses, and the added information of CT-FFR can change clinical decision-making in up to 66% of patients (25–28). Previous studies demonstrated that while a positive CT-FFR result (≤0.80) was associated with higher revascularization rates at ICA (20,27,29,30), a negative CT-FFR result was associated with cancellation or deferral of ICA in 61% of the patients without increased short-term adverse events (20,28,29,31,32), even

Table 3: Outcomes of Patients with Significant Stenosis by CAD-RADS Severity, Hemodynamic Significance, and Examination Location

					IP + ED (*n* = 331)			OP (*n* = 406)		
Parameter	All	Without CT-FFR	With CT-FFR	*P* Value	Without CT-FFR	With CT-FFR	*P* Value	Without CT-FFR	With CT-FFR	*P* Value
No. of cases	737	463	274		166	165		297	109	
CAD-RADS score				<.001			<.001			<.001
0–2	83/737 (11.3)	73/463 (15.8)	10/274 (3.6)		37/166 (22.3)	3/165 (1.8)		36/297 (12.1)	7/109 (6.4)	
3	258/737 (35.0)	59/463 (12.7)	199/274 (72.6)		0/166 (0.0)	107/165 (64.8)		59/297 (19.9)	92/109 (84.4)	
4A–5	383/737 (52.0)	318/463 (68.7)	65/274 (23.7)		128/166 (77.1)	48/165 (29.1)		190/297 (64.0)	17/109 (15.6)	
N	13/737 (1.8)	13/463 (2.8)	0/274 (0.0)		8/166 (4.8)	0/165 (0.0)		5/297 (1.7)	0/109 (0.0)	
ICA	243/737 (33.0)	181/243 (74.5)	62/243 (25.5)	.04*	112/166 (67.5)	55/165 (33.3)	.05*	69/297 (23.2)	7/109 (6.4)	.08*
≥70% stenosis	64/243 (26.3)	50/64 (78.1)	14/64 (21.9)		38/166 (22.9)	10/165 (6.1)		12/297 (4.0)	4/109 (3.7)	
≥90% stenosis	94/243 (38.7)	83/94 (88.3)	11/94 (11.7)		47/166 (28.3)	11/165 (6.7)		36/297 (12.1)	0/109 (0.0)	
PCI	123/737 (16.7)	97/123 (78.9)	26/123 (21.1)	.05*	39/166 (23.5)	19/165 (11.5)	.87*	58/297 (19.5)	7/109 (6.4)	.46*

Note.—Data are presented as counts, with percentages in parentheses. *P* values are comparing those who did and did not undergo CT-FFR analysis. CAD-RADS = Coronary Artery Disease Reporting and Data System (for the worst vessel), CT-FFR = CT fractional flow reserve, ED = emergency department, ICA = invasive coronary angiography, IP = inpatient, N = nondiagnostic (image quality is insufficient for making a reliable assessment), OP = outpatient, PCI = percutaneous coronary intervention.
* *P* value has been adjusted for confounders.

for patients older than 65 years old (33). Besides all the potential benefits of this emerging technology, widespread integration of CT-FFR into clinical workflows remains limited, and optimal approaches to selecting patients for CT-FFR analysis continue to be refined (34). In our independent study, not sponsored by the vendor, we assessed the feasibility of CT-FFR analysis using dual-source CT scans performed without heart rate control and its impact on clinical outcomes.

In our study, only 0.7% of the submitted coronary CTA procedures were rejected for CT-FFR analysis. This rejection rate was far lower than previously reported in the literature, ranging from 2.9% to 33% of the referrals (8,27,30). One reason for the low rejection rates in all cases is that since our program's inception almost 2 decades ago, all coronary CTA cases are reviewed while the patient is on the examination table; scans with artifacts are rectified (ECG editing, etc) and are repeated, if necessary (16). Although our standard dual-source coronary CTA protocol does not employ β-blockers for heart rate control, we noted a mean heart rate of 63 beats per minute (IQR: 55–76) in the group with CT-FFR analysis versus 65 beats per minute (IQR: 57–76) in the group without CT-FFR analysis (*P* = .10). Other characteristics of our standard of care include the use of automatic kilovoltage peak selection technology, routine inclusion of calcium scoring prior to all coronary CTA procedures to avoid underclassification (35) (but not cancellation of scans based on high calcium burden), and strong predilection for prospective ECG-triggering (and resultant overall reasonable radiation exposures). The high acceptance rate by the vendor obviated changing our existing imaging protocols (before implementation of CT-FFR, the only change we made [as advised by the vendor] was to reduce the level of iterative reconstruction strength by one step, from three of five to two of five vs our prior protocols).

In our current practice, CT-FFR referral is not mandated but instead initiated at the discretion of the interpreting physician on a case-by-case basis in situations where the analysis is thought to potentially change management, if successful. As expected, most referrals were for CAD-RADS grade 3 or greater stenoses. CT-FFR was requested in the majority (73.5%) of patients with CAD-RADS 3. In 27.7% of patients with CAD-RADS 3, cases were not sent because of vendor-dependent absolute or relative contraindications such as coronary stents and extensive coronary calcifications. We note that extensive calcifications are not a contraindication per the vendor and regulatory approval. Most of the remainder of CT-FFR referrals comprised focal CAD-RADS 4A disease; those ultimately not sent had similar contraindications or proceeded directly to ICA for further evaluation.

We acknowledge the higher proportion of studies with CT-FFR values above 0.80 in our study compared with the ADVANCE

Table 4: Image Quality Assessment Analysis

Parameter	Total	Excellent	Good	Fair	Poor	Nondiagnostic
Total	2985	7/2985 (0.2)	2644/2985 (88.6)	242/2985 (8.1)	50/2985 (1.7)	42/2985 (1.4)
Non–CT-FFR group	2693	6/2693 (0.2)	2392/2693 (88.8)	217/2693 (8.1)	40/2693 (1.5)	38/2693 (1.4)
CT-FFR group	292	1/292 (0.3)	252/292 (86.3)	25/292 (8.6)	10/292 (3.4)	4/292 (1.4)
P value		.51	.21	.73	.03	…
IP + ED (*n* = 1218)						
Without CT-FFR	1043	5/1043 (0.5)	880/1043 (84.4)	126/1043 (12.1)	16/1043 (1.5)	16/1043 (1.5)
With CT-FFR	171	0/171 (0.0)	161/171 (94.2)	8/171 (4.7)	2/171 (1.2)	0/171 (0.0)
P value		…	<.001	.003	…	.15
OP (*n* = 1767)						
Without CT-FFR	1650	1/1650 (0.1)	1502/1650 (91.0)	91/1650 (5.5)	24/1650 (1.5)	26/1650 (1.6)
With CT-FFR	113	0/113 (0.0)	103/113 (91.2)	5/113 (4.4)	5/113 (4.4)	0/113 (0.0)
P value		…	…	.83	.03	.41

Note.—Data are presented as counts, with percentages in parentheses. Of the patients referred to CT-FFR analysis, two studies were rejected and six analyses did not evaluate the lesion of concern. *P* values are comparing those who did and did not undergo CT-FFR analysis. CT-FFR = CT fractional flow reserve, ED = emergency department, ICA = invasive coronary angiography, IP = inpatient, OP = outpatient, PCI = percutaneous coronary intervention.

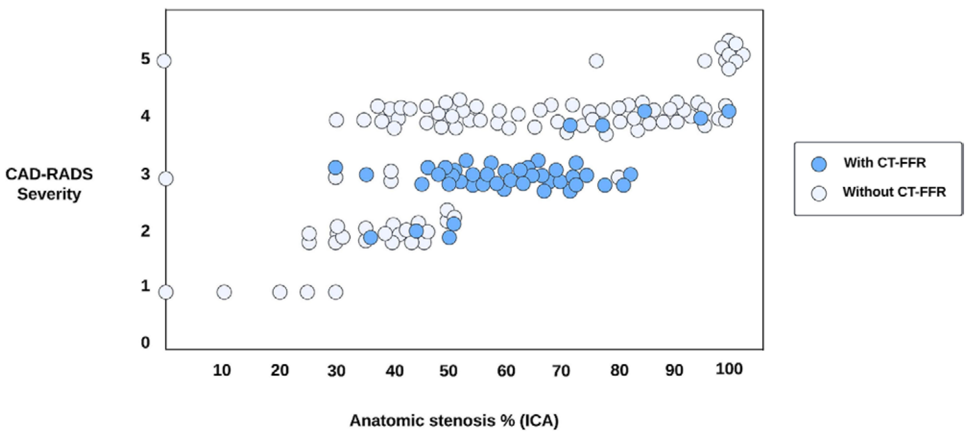

Figure 3: Correlation of CAD-RADS score with anatomic stenosis. CAD-RADS = Coronary Artery Disease Reporting and Data System, CT-FFR = CT fractional flow reserve, ICA = invasive coronary angiography.

registry (28). Our selection process involved CAD-RADS 3 lesions and some CAD-RADS 4 or greater lesions, based on clinical discretion. The variability in defining "moderate" stenosis, the pragmatic threshold used in our study, and differences in techniques across international sites may contribute to the observed differences. Additionally, variations in diameter stenosis definitions, coronary diameter measurements, and lesion configurations can further impact the results. These factors should be considered when interpreting and comparing our findings to other studies.

In our study, patients with significant stenosis at coronary CTA and a CT-FFR examination showed lower rates of ICA, PCI, and adverse cardiac events (all-cause death, myocardial infarction, ICA, or PCI within 3 months). Positive CT-FFR results were associated with higher rates of ICA and PCI for the same subset of patients. These results highlight the potential benefit of CT-FFR in decreasing the rate of ICA without compromising safety and are in agreement with the CT-FFR analysis of the PROMISE cohort (30), which showed that CT-FFR of 0.80 or less may improve the efficiency of referral to ICA compared with CTA alone.

This study had limitations. We acknowledge the potential for referral bias as a limitation of our study, as scans with satisfactory image quality were selectively chosen for CT-FFR analysis, which may introduce a bias toward higher acceptance rates. Our assessment of adverse outcomes by chart review may underestimate the true incidence due to the relatively short follow-up period and events that may have occurred outside our hospital system. In addition, although medical and prevention therapies are of substantial importance in patient care, this information was not part of our data collection, as our study's aim was focused on the performance of selective CT-FFR use and its effect on patient outcomes.

Conclusion

This study demonstrates the utility of CT-FFR in clinical practice, highlighting its potential to reduce the frequency of ICA and PCI in patients with significant coronary stenosis without compromising safety. The selective application of CT-FFR has shown to be feasible and beneficial. Future research could focus on the long-term outcomes of CT-FFR–guided decision-making and explore the integration of CT-FFR into broader clinical workflows, potentially including its use in patients with various ranges of coronary artery disease severity. This would further solidify the role of CT-FFR in the management of coronary artery disease and help refine patient selection criteria.

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