Radiology

ORIGINAL RESEARCH • CARDIAC IMAGING

Determinants of Rejection Rate for Coronary CT Angiography Fractional Flow Reserve Analysis

*Gianluca Pontone, MD, PhD** • *Jonathan R. Weir-McCall, MD** • *Andrea Baggiano, MD* • *Alberico Del Torto, MD* • *Laura Fusini, MD* • *Marco Guglielmo, MD* • *Giuseppe Muscogiuri, MD* • *Andrea Igoren Guaricci, MD, PhD* • *Daniele Andreini, MD, PhD* • *Manesh Patel, MD* • *Koen Nieman, MD* • *Takashi Akasaka, MD* • *Campbell Rogers, MD* • *Bjarne L. Nørgaard, MD* • *Jeroen Bax, MD* • *Gilbert L. Raff, MD* • *Kavitha Chinnaiyan, MD* • *Daniel Berman, MD* • *Timothy Fairbairn, MD* • *Lynne Hurwitz Koweek, MD* • *Jonathon Leipsic, MD*

From the Department of Cardiovascular Imaging, Centro Cardiologico Monzino, IRCCS, Via C. Parea 4, 20138 Milan, Italy (G.P., A.B., A.D.T., L.F., M.G., G.M., D.A.); Department of Radiology, School of Clinical Medicine, University of Cambridge, Cambridge, England (J.R.W.); Institute of Cardiovascular Disease, Department of Emergency and Organ Transplantation, University Hospital Policlinico of Bari, Bari, Italy (A.I.G.); Duke University School of Medicine, Durham, NC (M.P., L.H.K.); Department of Cardiology, Stanford University School of Medicine, Stanford, Calif (K.N.); Wakayama Medical University, Wakayama, Japan (T.A.); HeartFlow, Redwood City, Calif (C.R.); Department of Cardiology, Aarhus University Hospital, Aarhus Skejby, Denmark (B.L.N.); Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands (J.B.); William Beaumont Hospital, Royal Oak, Mich (G.L.R., K.C.); Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, Calif (D.B.); Liverpool Heart and Chest Hospital, Liverpool, England (T.F.); and Department of Radiology, University of British Columbia, Vancouver, Canada (J.L.). Received December 3, 2018; revision requested January 8, 2019; revision received April 8; accepted June 11. **Address correspondence to** G.P. (e-mail: *gianluca.pontone@ccfm.it*).

Supported by HeartFlow.

* G.P. and J.R.W. contributed equally to this work.

Conflicts of interest are listed at the end of this article.

See also the editorial by Sakuma in this issue.

Radiology 2019; 292:597–605 • https://doi.org/10.1148/radiol.2019182673 • Content codes: CA CT

Background: Coronary artery fractional flow reserve (FFR) derived from CT angiography (FFT_{CT}) enables functional assessment of coronary stenosis. Prior clinical trials showed 13%–33% of coronary CT angiography studies had insufficient quality for quantitative analysis with FFR_{CT}.

Purpose: To determine the rejection rate of FFR_{CT} analysis and to determine factors associated with technically unsuccessful calculation of FFR_{CT}.

Materials and Methods: Prospectively acquired coronary CT angiography scans submitted as part of the Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care (ADVANCE) registry (*https://ClinicalTrials.gov:* NCT02499679) and coronary CT angiography series submitted for clinical analysis were included. The primary outcome was the FFR_{CT} rejection rate (defined as an inability to perform quantitative analysis with FFR_{CT}). Factors that were associated with FFR_{CT} rejection rate were assessed with multiple linear regression.

Results: In the ADVANCE registry, FFR_{CT} rejection rate due to inadequate image quality was 2.9% (80 of 2778 patients; 95% confidence interval [CI]: 2.1%, 3.2%). In the 10 621 consecutive patients who underwent clinical analysis, the FFR_{CT} rejection rate was 8.4% (n = 892; 95% CI: 6.2%, 7.2%; $P < .001$ vs the ADVANCE cohort). The main reason for the inability to perform FFR_{CT} analysis was the presence of motion artifacts (63 of 80 [78%] and 729 of 892 [64%] in the ADVANCE and clinical cohorts, respectively). At multivariable analysis, section thickness in the ADVANCE (odds ratio [OR], 1.04; 95% CI: 1.001, 1.09; $P = .045$) and clinical (OR, 1.03; 95% CI: 1.02, 1.04; $P < .001$) cohorts and heart rate in the ADVANCE (OR, 1.05; 95% CI: 1.02, 1.08; $P < .001$) and clinical (OR, 1.06; 95% CI: 1.05, 1.07; $P < .001$) cohorts were independent predictors of rejection.

Conclusion: The rates for technically unsuccessful CT-derived fractional flow reserve in the ADVANCE registry and in a large clinical cohort were 2.9% and 8.4%, respectively. Thinner CT section thickness and lower patient heart rate may increase rates of completion of CT fractional flow reserve analysis.

Online supplemental material is available for this article.

Coronary artery disease is a major cause of mortality and morbidity, and its management consumes a large portion of health care budgets (1). Several noninvasive tests are commonly used as gatekeepers to invasive coronary angiography. Despite the frequent use of noninvasive functional stress testing, the prevalence of obstructive coronary artery disease at elective invasive coronary angiography is low (2,3).

Coronary CT angiography is an alternative anatomically based imaging modality used to assess coronary artery disease. However, because of its limited positive predictive value, it can lead to increased downstream use of invasive coronary angiography (4–6). Recently, participant-specific coronary CT angiography data have been combined with computational fluid dynamic models, allowing for noninvasive determination of the fractional flow reserve derived from coronary CT angiography (FFR_{CT}). This correlates well with invasive FFR and reduces rates of invasive coronary angiography use compared with coronary CT angiography alone (7,8). In these previous trials,

Abbreviations

ADVANCE = Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, CI = confidence interval, DICOM = Digital Imaging and Communications in Medicine, FFR = fractional flow reserve, FFR_{CT} = FFR derived from coronary CT angiography, HR = heart rate, OR = odds ratio, ROU = region of uninterpretability

Summary

Both the Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, or ADVANCE, cohort and the clinical cohort of more than 10 000 patients showed relatively low rates for technically unsuccessful calculation of CT fractional flow reserve (2.9% and 8.4%, respectively).

Key Points

- Analysis of contemporary databases shows CT fractional flow reserve (FFR) from coronary CT angiography studies had relatively low rates for technically unsuccessful studies (range, 2.9%–8.4%).
- Contemporary CT angiography made greater use of dual-source technology and wide-coverage single-source scanners than did prior clinical trials.
- In the Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, or ADVANCE, and clinical cohorts, greater CT section thickness (odds ratio, 1.04 and 1.03, respectively) and higher patient heart rate (odds ratio, 1.05 and 1.06, respectively) were associated with an inability to perform CT-derived FFR analysis.

FFR_{CT} analysis could be performed in 87%–88% of coronary CT angiography data sets (7,8); however, a more recent substudy of the Prospective Multicenter Imaging Study for Evaluation of Chest Pain, or PROMISE, trial found that because of low-quality images, only 67% of coronary CT angiography data sets could be used for FFR_{CT} analysis (9). Previous studies have examined the factors that affect the accuracy of FFR_{CT} (for instance, both nitrate use and β-blocker use improve diagnostic accuracy) (10,11). However, factors that affect the ability to perform FFR_{CT} analysis of coronary CT angiography data remain poorly understood. Identification of such factors would allow for targeted intervention to increase the likelihood of using this additional analysis in clinical care.

Thus, the aim of our study was to examine the rejection rate of coronary CT angiography for FFR_{CT} analysis and the factors associated with an inability to perform FFR_{CT} in the controlled Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care (ADVANCE) registry (12) and in an uncontrolled cohort of clinical cases.

Materials and Methods

This study was conducted in accordance with the Declaration of Helsinki. Participants in the ADVANCE registry all provided written informed consent. The clinical cohort analysis was performed with anonymized metadata. Institutional review board approval and patient consent were obtained at all sites and from all participants in the ADVANCE registry. For the commercial cases, all sites provided local institutional review board approval to publish any metadata available from the FFR_{CT} submission. HeartFlow served as a sponsor of the ADVANCE registry (*https://ClinicalTrials.gov*: NCT02499679). All data in the study were held by the authors, and data analysis, reporting, and submission were performed independent of the sponsor.

Study Cohorts

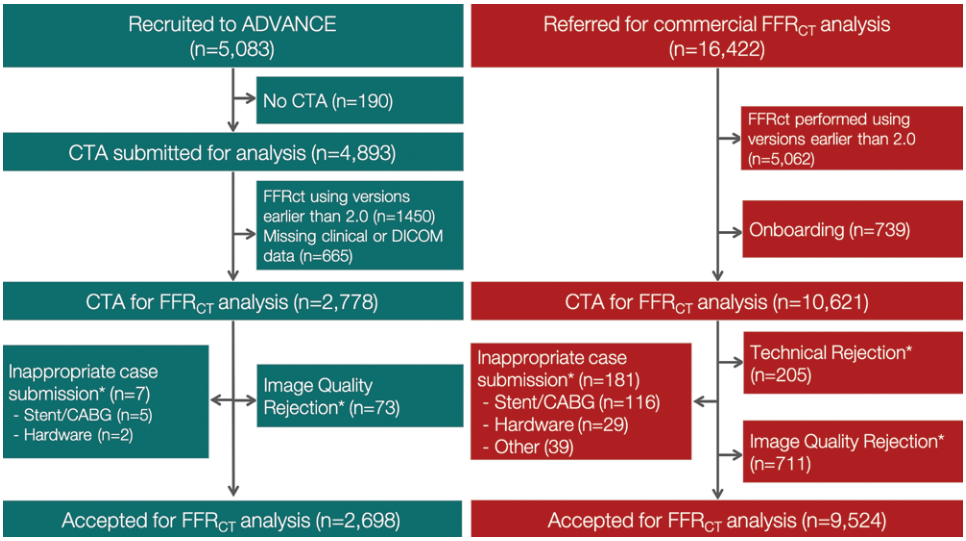
ADVANCE registry.—The ADVANCE registry is a multicenter prospective controlled registry; patients were recruited for inclusion from July 15, 2015, to October 20, 2017. The ADVANCE registry was designed to evaluate clinical utility, outcomes, and resource use after FFR_{CT}-guided treatment in clinically stable symptomatic patients with a coronary artery disease diagnosis at coronary CT angiography (12,13). The inclusion and exclusion criteria have been previously published and are available in Figures E1–E3 (online) (14). Analyses performed using FFR_{CT} analysis software (version 2.0 or higher) were included in the current analysis; 1450 analyses performed using software versions older than version 2.0 were excluded. Version 2.0 or higher software was used because these are the versions that are currently used in clinical care; thus, they are the most generalizable to current practice.

Clinical submission cohort.—All patients referred for clinical consecutive coronary CT angiography between July 2016 and March 2018 and who had FFR_{CT} analysis performed with version 2.0 or higher FFR_{CT} analysis software were considered for inclusion. Before this point, 5062 cases in the clinical cohort were analyzed with software versions older than 2.0 and were not included in the current study. There was no overlap of participants in the clinical cohort with those in the ADVANCE cohort. All coronary CT angiography examinations were performed according to the local policy of the referring center. When a scan was rejected for analysis, a reason was included in the rejection notification to the referring center. If this could be modified, the case could then be resubmitted. Only the final accepted scans were included. The rationale for this was that if a scan could be amended and subsequently processed, it was simply a postprocessing issue, whereas the rejections that were not amenable to such simple steps were of interest because they represented a lost opportunity.

During the initial commercial set-up, there is an intensive process for the first few weeks, during which structured education and feedback are provided to ensure optimization of the data submitted for analysis; this is referred to as *onboarding*. Centers that were still onboarding at the end of the study period and all scans performed during the onboarding process (n = 739) were excluded from this study.

FFR_{CT} analysis.—The decision to refer a patient for FFR_{CT} analysis was made by the physician interpreting the coronary CT angiography images. All FFR_{CT} analysis was performed at a single center (HeartFlow). Analysis was performed as previously described (15).

DICOM data extraction.—From the Digital Imaging and Communications in Medicine (DICOM) metadata of the submitted coronary CT angiography scan, information on patient



Flow diagram of the study participants in both cohorts. ∗ The number of cases is greater than the total number of rejections, as cases could be rejected for more than one reason. *Technical rejection* means all automatic rejections were due to the data failing to meet minimum technical specifications for fraction flow reserve derived from coronary CT angiography (FFR_{CT}) analysis due to data format. *Image quality rejection* means image quality was inadequate to allow for generation of the anatomic coronary model necessary for FFR_{CT} calculation. ADVANCE = Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, CABG = coronary artery bypass graft, CTA = CT angiography, DICOM = Digital Imaging and Communications in Medicine.

and technical factors was extracted. The patient factors obtained were heart rate (HR) and HR variability. The technical factors obtained included scanner type, number of sources, number of sections, section thickness, pixel spacing (distance between the center of the pixel in the x-y plane, which in turn is determined by the reconstructed field of view), temporal resolution, tube voltage, aortic attenuation, aortic noise, and effective radiation dose measured as the product of dose-length product times for conversion coefficient for the chest (K = 0.026 mSv/mGy·cm) (16). From the DICOM imaging data, aortic contrast material opacification was calculated as the mean attenuation (in Hounsfield units) within the aortic root volume extracted for FFR_{CT} analysis, while image noise was measured as the standard deviation of Hounsfield units within the same volume of the aortic root. The signal-to-noise ratio was calculated as the mean attenuation (in Hounsfield units) in the aorta divided by the standard deviation of attenuation in the aorta. The pixel spacing contained within the DICOM metadata was used to back-calculate the reconstructed field of view, as this is the more intuitive and clinically appreciable input metric. This was done by multiplying the pixel spacing by 512 to coincide with the size of the CT output matrix.

End point.—Rate of coronary CT angiography rejection for FFR_{CT} analysis was defined as the inability of technologists at HeartFlow, who were blinded to the clinical data, to perform FFR_{CT} analysis. The reason for rejection was recorded and classified as follows: *(a)* Technical rejection included all automatic rejections due to the data failing to meet minimum technical specifications for FFR_{CT} analysis due to data format. Reasons for technical rejection are as follows: section thickness or spacing of 1 mm or greater, pixel size of 0.5 mm or greater (equivalent to a reconstructed field of view ≥25.6 cm), or missing data. *(b)* Rejection due to inappropriate submission included all cases in which FFR_{CT} was not validated for clinical use and therefore was not suitable for analysis. This included a previous history of revascularization (stent or coronary artery bypass graft) or patients who had missing coronary or cardiac segments due to inadequate scan range, inappropriate field of view reconstruction (clipped structure), or inappropriate section thickness. *(c)* Image quality rejections included cases in which image quality was inadequate to allow for generation of the anatomic coronary model necessary for FFR_{CT} calculation. This decision was made based on two parallel assessments. The first was an image quality scoring system of the coronary arteries in which the length of the artifact, diameter of the vessel in which the artifact is present, whether a stenosis is present within the region of the artifact, and the type of artifact were combined and weighted according to the location of the artifact within the vessel, with more proximal artifacts given greater weighting. Scans with an inadequate image quality score were rejected. The second related decision process was based on the presence of any regions of uninterpretability (ROUs). Cases were not processed if one vessel system contained two ROUs longer than 5 mm, all three vessel systems contained one ROU longer than 5 mm, or one vessel system contained one ROU longer than 30 mm. If a scan failed because of the image quality or the ROU criteria, it was rejected. *(d)* For these patients, the reason for poor image quality was recorded as blooming artifact, motion artifact, or image noise. Examples of coronary CT angiography studies rejected for inadequate image quality are shown in Figures E1–E3 (online).

These criteria have remained stable since software was updated from version 1.6 through version 2.0 or higher. DICOM data from technical rejections are not stored and are not available for analysis.

Statistical Analysis

Statistical analysis was performed with statistical software (SPSS, version 23, SPSS, Chicago, Ill; R, version 2.15.2, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean ± standard deviation or median and 25th to 75th percentile, as appropriate. Discrete variables were expressed as absolute numbers and percentages. Student independent *t* tests or Mann-Whitney tests were used, as appropriate, to compare continuous variables among pa-

Table 1: Baseline Characteristics of the ADVANCE Registry

Variable	All Patients (n = 2778)	FFR_{CT} Completed (n = 2698)	FFR_{CT} Rejected (n = 80)	P Value
Demographic characteristic				
Age (y)	66 ± 10	66 ± 10	68 ± 12	.178
No. of men	1845 (66)	1796 (67)	49 (61)	.321
Body mass index (kg/m^2)	26.3 ± 4.8	26.3 ± 4.8	26.9 ± 5.6	.292
Cardiovascular risk factor				
Smoking history	1693 (61)	1632 (61)	61 (76)	.004
Hyperlipemia	1702 (61)	1651 (61)	51 (64)	.644
Diabetes	619 (22)	592 (22)	27 (34)	.012
All symptoms				
Unknown	22 (1)	21 (1)	1 (1)	.639
None	742 (27)	727 (27)	15 (19)	.103
Noncardiac chest pain	169 (6)	166 (6)	3 (4)	.376
Dyspnea	303 (11)	295 (11)	8 (10)	.792
Atypical angina	1020 (37)	982 (36)	38 (48)	.042
Typical angina	522 (19)	507 (19)	15 (19)	.992
Symptoms clustered	…	…	…	.050
Other	1236 (44)	1209 (45)	27 (34)	…
Angina	1542 (56)	1489 (55)	53 (66)	…
Coronary CT angiography characteristic				
Scanner manufacturer	…	…	…	<.001
GE Medical Systems	523 (19)	511 (19)	12 (15)	…
Siemens	1641 (59)	1602 (59)	39 (49)	…
Philips	192 (7)	174 (6)	18 (23)	…
Toshiba	422 (15)	411 (15)	11 (14)	…
No. of sources	…	…	…	.004
Single	1507 (54)	1451 (54)	56 (70)	…
Dual	1271 (46)	1247 (46)	24 (30)	…
CT scanner detector coverage clustered	…	…	…	.98
<16 cm	1706 (61)	1657 (61)	49 (61)	…
≥16 cm	1072 (39)	1041 (39)	31 (39)	…
Temporal resolution	106 ± 37	106 ± 37	119 ± 36	.001
Tube voltage (kVp)	109 ± 15	108 ± 15	115 ± 13	<.001
Tube voltage clustered	…	…	…	.003
Low (<100 kVp)	1381 (50)	1354 (50)	27 (34)	…
Medium (100–120 kVp)	1253 (45)	1209 (45)	44 (55)	…
High (>120 kVp)	144 (5)	135 (5)	9 (11)	…
Aorta contrast attenuation (HU)	465.2 ± 126.2	466.4 ± 126.4	422.1 ± 111.7	.002
Image noise (HU)	87.7 ± 34.0	87.9 ± 34.1	82.2 ± 32.4	.141
Signal-to-noise ratio	5.88 ± 2.06	5.88 ± 1.99	6.00 ± 3.76	.77
Reconstructed field of view (cm)	18.5 ± 29.5	18.4 ± 29.3	19.3 ± 35.5	.031
Section thickness (mm)	0.64 ± 0.10	0.64 ± 0.10	0.67 ± 0.11	.008
Dose (mSv)	10.0 ± 9.1	9.9 ± 9.1	13.9 ± 10.0	.001
Heart rate (beats/min)	60 ± 9	60 ± 9	63 ± 14	.032
Heart rate variability (beats/min)	15 ± 30	15 ± 30	17 ± 23	.686
Coronary dominance	…	…	…	.785
Right	1868 (67)	1816 (67)	52 (65)	…
Left	234 (8)	228 (8)	6 (7)	…
Codominant	676 (24)	654 (24)	22 (28)	…

Note.—Continuous variables with normal distribution are expressed as mean ± standard deviation. Discrete variables are expressed as absolute number, with the percentage in parentheses. ADVANCE = Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, FFR_{CT} = fractional flow reserve calculated from CT.

Table 2: Baseline Characteristics of the Clinical Cohort

Variable	All Patients (n = 10416)	FFR_{CT} Completed (n = 9524)	FFR_{CT} Rejected (n = 892)	P Value
Manufacturer	…	…	…	<.001
GE Medical Systems	3278 (32)	2982 (31.3)	296 (33.2)	…
Siemens	4125 (40)	3822 (40.1)	303 (34.0)	…
Philips	1456 (14)	1283 (13.5)	173 (19.4)	…
Toshiba	1542 (15)	1423 (14.9)	119 (13.3)	…
No. of x-ray sources	…	…	…	<.001
Single source	7025 (67)	6344 (66.6)	681 (76.3)	…
Dual source	3343 (33)	3137 (32.9)	206 (23.1)	…
CT scanner detector coverage				
<16 cm	5594 (54)	5071 (54)	523 (59)	…
≥16 cm	4774 (46)	4410 (46)	364 (41)	.002
Temporal resolution (msec)	120 ± 39	119 ± 39	130 ± 38	<.001
Tube voltage (kVp)	112 ± 12	112 ± 12	116 ± 11	<.001
Tube voltage categories	…	…	…	<.001
Low (<100 kVp)	587 (5.6)	575 (6.0)	22 (2.5)	…
Medium (100–120 kVp)	9436 (91)	8622 (90.5)	814 (91.3)	…
High (>120 kVp)	371 (3.5)	316 (3.3)	55 (6.2)	…
Aorta contrast opacification (HU)	445.4 ± 134.2	450.4 ± 134.0	392.0 ± 125.0	<.001
Image noise (HU)	98.8 ± 37.0	98.8 ± 36.7	98.9 ± 39.7	.96
Signal-to-noise ratio in the aorta	5.05 ± 1.95	5.10 ± 1.95	4.49 ± 1.80	<.001
Reconstructed field of view (cm)	20.7 ± 27.5	20.6 ± 27.4	21.6 ± 26.3	<.001
Section thickness (mm)	0.63 ± 0.10	0.63 ± 0.09	0.65 ± 0.10	<.001
Radiation dose (mSv)	9.9 ± 7.8	9.5 ± 7.4	13.8 ± 10.4	<.001
Heart rate (beats/min)	60 ± 9	60 ± 9	65 ± 12	<.001
Heart rate variability (beats/min)	17 ± 30	17 ± 29	24 ± 42	.001

Note.—Continuous variables with normal distribution are expressed as mean ± standard deviation. Discrete variables are expressed as absolute number, with the percentage in parentheses. FFR_{CT} = fractional flow reserve calculated from CT.

tients in whom FFR_{CT} analysis was performed versus those who were rejected for FFR_{CT} analysis. Comparisons among groups of discrete variables were performed by using the χ^2 or Fisher exact test if the expected cell count was less than five. Binary logistic regression was used to assess the association between baseline covariates and FFR_{CT} rejection (results are presented as odds ratio [OR] and 95% confidence interval [CI]). Variables with $P < .1$ at univariable analysis were then included as covariates in multivariable analysis. All tests were two tailed, and $P < .05$ was considered to indicate a significant difference.

Results

Cohort Characteristics

This study included 2778 participants from the ADVANCE registry (1845 [66%] were men; mean age of the total cohort, 66.2 years ± 10.3; mean age of men, 65.1 years ± 10.2; mean age of women, 68.5 years ± 10.0; $P < .001$ for between-sex age difference) and 10621 participants from the clinical cohort. A flow diagram of the study participants can be found in the Figure. The characteristics of the cohorts are listed in Tables 1 and 2.

ADVANCE Registry

Scans of the 2778 participants were submitted from 38 sites in Europe, North America, and Japan. Coronary CT angiography was performed using 16 scanner models produced by four different manufacturers: GE Healthcare (n = 523 [19%]), Siemens (n = 1641 [59%]), Philips (n = 192 [7%]), and Toshiba (n = 422 [15%]). The majority of scans were performed with single-source units (n = 1507 [54%]), a substantial portion of which were wide-coverage CT scanners (n = 1072 [39%]) (Table 1). A low tube potential (≤100 kVp) was used in 1381 of 2778 (50%) participants (Table 1). The mean HR and HR variability were 60 beats per minute ± 9 and 15 beats per minute ± 30, respectively, with a mean dose of 10.0 mSv ± 9.1 (Table 1).

The rejection rate was 80 of 2778 participants (2.9%; 95% CI: 2.32%, 3.57%). Of the 2778 participants, 73 (2.62%; 95% CI: 2.06%, 3.25%) were rejected for inadequate image quality, and the other seven (0.25%; 95% CI: 0.15%, 0.57%) were rejected due to inappropriate case submission (Table 3). Rejection of coronary CT angiography scans for FFR_{CT} analysis was greater in patients with a history of smoking, diabetes, or angina (Table 1). Technical factors associated with coronary CT angiography rejection for FFR_{CT} analysis were lower use of dual-source CT scanning, lower aorta contrast, wider reconstructed field of view, and greater section thickness (Table 1). Finally, HR was higher in the rejected cases than in the accepted cases (63 beats per minute ± 14 vs 60 beats per minute ± 9, P = .03), with no difference in HR variability between groups.

Tables 4 and 5 show uni- and multivariable analysis of factors associated with rejection for analysis in the ADVANCE registry. In the fully adjusted model, smoking history (smokers vs

Table 3: Reason for FFR_{CT} Rejection in the ADVANCE Registry and Clinical Cohort

Reason for Rejection	FFR_{CT} Rejected*	
	ADVANCE Registry (n = 80)	Clinical Cohort (n = 892)
Inadequate image quality†		
Blooming	4 (5.0)	29 (3.0)
Clipped structure	4 (5.0)	39 (4.3)
Motion artifacts	63 (78.0)	729 (81.4)
Image noise	2 (2.5)	198 (22.1)
Inappropriate submission		
Stent or previous coronary artery bypass graft present	5 (6.2)	116 (13.0)
Cardiac hardware present	2 (2.5)	29 (3.2)

Note.—Discrete variables are expressed as absolute number, with the percentage in parentheses. ADVANCE = Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, FFR_{CT} = fractional flow reserve derived from CT.

* Values are greater than the total number of rejections because scans can be rejected for more than one reason.

† Inadequate image quality is based on *(a)* length of the artifact, diameter of the vessel in which the artifact is present, whether a stenosis is present within the region of artifact, and the type of artifact is weighted according to the location of the artifact and *(b)* the presence of any regions of uninterpretability (ROUs). Cases are not processed if one vessel system contains two ROUs longer than 5 mm, if all three vessel systems contain one ROU longer than 5 mm, or if one vessel system contains one ROU longer than 30 mm.

nonsmokers: OR, 2.7; 95% CI: 1.2, 5.6; P = .01), temporal resolution (<100 msec vs ≥100 msec: OR, 2.7; 95% CI: 1.3, 5.6; P = .006), section thickness (per 0.01-mm increase in section thickness: OR, 1.04; 95% CI: 1.0, 1.09; P = .045), and HR (per beat per minute increase in HR: OR, 1.05; 95% CI: 1.02, 1.08; P < .001) were all independent predictors of rejection (Table 5).

Clinical Cohort

A total of 10621 cases were submitted for FFR_{CT} analysis between July 2016 and November 2017. A total of 205 submissions were automatically rejected due to the DICOM files not meeting the minimum technical data specifications. Therefore, the final population comprised 10416 patients. The cases were submitted by 76 centers (median, 78 scans per center; range, one to 884 scans) covering 10 countries in North America, Europe, and Asia. These were performed by using 22 CT scanner models produced by four different manufacturers—GE Healthcare (3278 scans [32%]), Siemens (4125 scans [40%]), Philips (1456 scans [14%]), and Toshiba (1542 scans [15%])—with the majority being performed with single-source units (7025 scans [67%]). Low-tube potential (≤100 kVp) was used in 587 participants (5.6%) (Table 2). The mean HR and HR variability were 60 beats per minute ± 9 and 17 beats per minute ± 30, respectively, with a mean dose of 9.9 mSv ± 7.8 (Table 2).

The rejection rate was 892 of 10416 cases submitted (8.60%; 95% CI: 7.89%, 8.93%). Of the 10416 cases, 711 (6.8%; 95% CI: 6.23%, 7.18%) were rejected for inadequate image quality; the remainder were rejected for technical limitations of the submitted data or because of the presence of stents, bypass grafts, or other cardiac hardware (Table 3). The coronary CT angiography rejection rate was higher in the clinical cohort than in the ADVANCE registry (P < .001).

Participants in whom the coronary CT angiography scan was rejected for FFR_{CT} analysis showed a lower use of dual-source and wide-coverage CT scanners, lower aorta contrast, wider reconstructed fields of view, and greater section thickness as compared with participants in whom coronary CT angiography scans were accepted (P < .001 for all) (Table 2). Participants in whom the coronary CT angiography scan was rejected had a higher HR (mean, 65 beats per minute ± 12 vs 60 beats per minute ± 9; P < .001) and a higher HR variability (mean, 24 beats per minute ± 42 vs 17 beats per minute ± 29; P = .001) compared with those in whom the coronary CT angiography scan was accepted (Table 2). When considering only wide-detector and dual-source CT scanners, dual-source CT scanners were associated with lower rates of coronary CT angiography rejection for FFR_{CT} (wide detector, 364 of 4774 [7.6%] vs dual source, 206 of 3343 [6.2%]; P = .01). This difference remained when only wide-detector scanners with temporal resolution of less than 140 msec were considered (wide detector, 245 of 2675 [9.2%] vs dual source, 206 of 3343 [6.2%]; P < .001).

Tables 4 and 5 show uni- and multivariable analysis of the factors associated with coronary CT angiography rejection in the clinical cohort. At multivariable analysis, section thickness (per 0.01-mm increase: OR, 1.03; 95% CI: 1.02, 1.04; P < .001), HR (per beat per minute increase: OR, 1.06; 95% CI: 1.05, 1.07; P < .001), wide volume scanner coverage (≥16 cm vs <16 cm: OR, 0.47; 95% CI: 0.39, 0.58; P < .001), scanner temporal resolution (≥100 msec vs <100 msec: OR, 1.7; 95% CI: 1.4, 2.1; P < .001), higher aortic contrast opacification (per increase in Hounsfield units: OR, 0.997; 95% CI: 0.996, 0.998; P < .001), and a wider reconstructed field of view size (per 1-cm increase: OR, 1.01; 95% CI: 1.007, 1.0013; P < .001) were independently associated with coronary CT angiography scan rejection.

Discussion

The main findings of our study are that the rate of rejection of coronary CT angiography scans for fractional flow reserve derived from coronary CT angiography (FFR_{CT}) analysis due to inadequate image quality is low, and it is lower in the Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care (ADVANCE) cohort than in the clinical cohort. We also found temporal resolution, section thickness, and heart rate (HR) are independent predictors of coronary CT angiography scan rejection for FFR_{CT} analysis.

The observed rate of coronary CT angiography rejection for FFR_{CT} analysis was significantly lower than that reported in the published literature, where it ranges from 13% to 33% (7,9). The reason for the low rate of rejection in our study may be related to the greater use of dual-source technology and wide-coverage

Table 4: Univariable Predictors of FFR_{CT} Rejection in the ADVANCE Registry and Clinical Cohort

	ADVANCE Registry		Clinical Cohort	
Variable	Odds Ratio	*P* Value	Odds Ratio	*P* Value
Demographic characteristic				
Age (y)	1.01 (0.99, 1.04)	.18	…	…
No. of men	1.3 (0.8, 1.9)	.32	…	…
Body mass index (kg/m²)	1.0 (1.0, 1.1)	.29	…	…
Cardiovascular risk factor				
Smoking history	2.1 (1.3, 3.5)	.005	…	…
Hyperlipemia	1.1 (0.7, 1.8)	.64	…	…
Diabetes	1.8 (1.1, 2.9)	.01	…	…
All symptoms				
Unknown	1.6 (0.2, 12.1)	.64	…	…
None	0.6 (0.4, 1.1)	.11	…	…
Noncardiac chest pain	0.6 (0.2, 1.8)	.38	…	…
Dyspnea	0.9 (0.4, 1.9)	.79	…	…
Atypical angina	1.6 (1.9, 2.5)	.04	…	…
Typical angina	1.0 (0.6, 1.8)	.99	…	…
Clustered symptoms	1.6 (1.0, 2.2	.052	…	…
Coronary CT angiography characteristic				
Detector coverage				
< 16 cm	…	…	…	…
≥16 cm	1.0 (0.6, 0.1.6)	.98	0.80 (0.70, 0.92)	.002
Temporal resolution				
High (<100 msec)	…	…	…	…
Low-medium (≥100 msec)	2.1 (1.4, 3.2)	.001	1.6 (1.4, 1.9)	<.001
Tube voltage				
Low (<100 kVp)	…	…	…	…
Medium (100–120 kVp)	1.8 (1.1, 3.0)	.01	2.5 (1.60, 3.80)	<.001
High (>120 kVp)	3.3 (1.5, 7.3)	.002	4.6 (2.72, 7.60)	<.001
Aorta contrast opacification (HU)	1.0 (0.995, 0.99)	.002	0.996 (0.996, 0.997)	<.001
Image noise (HU)	1.0 (0.98, 1.0)	.14	1.0 (0.998, 1.002)	.95
Signal-to-noise ratio	1.0 (0.93, 1.1)	.59	0.9 (0.8, 0.9)	<.001
Reconstructed field of view (cm)	1.1 (1.0, 1.1)	.009	1.014 (1.01, 1.02)	<.001
Section thickness (per 0.01 mm)	1.0 (1.01, 1.1)	.009	1.02 (1.01, 1.03)	<.001
Dose (mSv)	1.1 (1.03, 1.11)	.001	1.1 (1.09, 1.12)	<.001
Heart rate (beats/min)	1.0 (1.01, 1.1)	.001	1.1 (1.05, 1.06)	<.001
Heart rate variability (beats/min)	1.0 (0.99, 1.01)	.69	1.01 (1.003, 1.008)	<.001
Coronary dominance				
Right	…	…	…	…
Left	0.9 (0.4–2.1)	.85	…	…
Codominant	1.2 (0.7–2.0)	.53	…	…

Note.—Some data are missing because they were not available in both datasets. Data in parentheses are the 95% confidence interval. ADVANCE = Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, FFR_{CT} = fractional flow reserve calculated from CT.

single-source scanners. Previous studies with dual-source technology show that image quality is less dependent on HR as compared to 64-section single-source coronary CT (17,18) and that wide-coverage scanner technology allows for single-beat whole-heart acquisition, reducing the occurrence of motion or step artifacts (19,20). Despite these advances in CT hardware over the past 2 decades, HR continues to be closely associated with image quality at coronary CT angiography (21). Coronary CT angiography performed using these scanners accounted for only 17% of scans in the PROMISE FFR_{CT} substudy, which had a 33% rejection rate (9). In our study, 85% of cases in the ADVANCE registry and 79% of the clinical cases submitted for analysis were performed with these types of scanners. An additional explanation for the difference observed between our study and the PROMISE FFR_{CT} substudy is that only 67% of CT angiography data sets met Society of Cardiovascular Computed Tomography, or SCCT, guidelines, yielding a higher rejected rate.

The main reason for FFR_{CT} rejection in our study was motion artifacts. In the Diagnostic Accuracy of Fractional Flow Reserve from Anatomic CT Angiography, or DEFACTO, trial, misalignment artifacts resulted in impaired sensitivity and

Table 5: Multivariable Predictors of FFR_{CT} Rejection of the ADVANCE Registry and Clinical Cohort

	ADVANCE Registry		Clinical Cohort*	
Variable	Odds Ratio	*P* Value	Odds Ratio	*P* Value
Smoking history	2.7 (1.2, 5.6)	.01	…	…
Diabetes	1.1 (0.5, 2.0)	.83	…	…
Detector coverage				
<16 cm	…	…	…	…
≥16 cm	…	…	0.5 (0.4, 0.6)	<.001
Temporal resolution				
High (<100 msec)	…	…	…	…
Low-medium (>100 msec)	2.7 (1.3, 5.6)	.01	1.7 (1.4, 2.1)	<.001
Tube voltage				
Low (<100 kVp)	…	…	…	…
Medium (100–120 kVp)	1.2 (0.5, 2.7)	.60	1.4 (0.8, 2.3)	.21
High (>120 kVp)	2.8 (0.8, 9.7)	.01	1.9 (1.02, 3.5)	.04
Aorta contrast opacification (HU)	1.0 (0.99, 1.00)	.11	0.997 (0.996, 0.998)	<.001
Reconstructed field of view (cm)	1.0 (0.99, 1.01)	.48	1.01 (1.007, 1.013)	<.001
Section thickness (per 0.01 mm)	1.04 (1.001, 1.09)	.045	1.03 (1.02, 1.04)	<.001
Dose (mSv)	1.03 (0.96, 1.1)	.43		
Heart rate (beats/min)	1.05 (1.02, 1.08)	<.001	1.06 (1.05, 1.07)	<.001

Note.—Data in parentheses are 95% confidence intervals. ADVANCE = Assessing Diagnostic Value of Noninvasive FFR_{CT} in Coronary Care, FFR_{CT} = fractional flow reserve calculated from CT.

* Heart rate variability and dose were excluded from multivariable analysis in the clinical cohort, as one or the other were not routinely collected with the Digital Imaging and Communications software of GE Healthcare, Philips, and Toshiba scanners, and this would have introduced a systematic bias in the results. A total of 7867 cases were included in the model due to missing variables in some cases.

overall accuracy of FFR_{CT}, while use of β-blockers yielded higher FFR_{CT} specificity (10). These findings support close adherence to the current guidelines for coronary CT angiography (22,23). Unfortunately, previous studies showed that adherence to these guidelines is variable and that the ideal HR for coronary CT angiography is achieved in only 55% of patients (17,24).

For both cohorts in our study, section thickness and pixel size showed a clear association with rejection of FFR_{CT} analysis. Given that greater section thickness and pixel size have reduced image noise (25), it may be that the cardiac imagers are selecting settings to improve image quality for visual analysis. However, peak aortic enhancement is a more important contributor than image noise for the ability to perform FFR_{CT} analysis, as evidenced by our observation that lower contrast opacification but not greater image noise was associated with rejection. Thus, it may be beneficial to reconstruct studies undergoing FFR_{CT} analysis with a small field of view and the smallest possible section thickness.

Our result showing that the ADVANCE cohort had a lower rate of coronary CT angiography rejection than the clinical cohort warrants consideration. Aortic contrast opacification was a significant predictor of rejection in the clinical cohort but not in the ADVANCE registry. Tube potential is an easily amendable scanning factor that boosts intravascular contrast opacification as it moves the kilovoltage peak closer to the k-edge of iodine; however, low-kilovoltage-peak scanning was implemented in only 6% of the clinical cases, whereas it was implemented in 50% of the ADVANCE cases, suggesting that optimizing scanner parameters eliminates suboptimal aortic contrast opacification. The reconstructed field of view was associated with rejection in the clinical cohort but not in ADVANCE cohort. The reconstructed field of view was 10% smaller in the ADVANCE cohort (18.5 cm) than in the clinical cohort (20.7 cm), suggesting a reticence of the clinical referral centers to optimally crop the images for cardiac analysis, presumably because they feared cropping out the coronary arteries or cardiac chambers.

Our study had some limitations. A referral bias is likely present, as referring cardiac imagers were unlikely to submit visually nondiagnostic coronary CT angiography scans for consideration for FFR_{CT}. Thus, our study most likely represents the percentage of visually diagnostic coronary CT angiography scans amenable to subsequent FFR_{CT} analysis rather than the percentage of all coronary CT angiography scans that are amenable to FFR_{CT} analysis. Moreover, there will be differences between the ADVANCE cohort and the clinical cohort, and the results of the two populations cannot be considered interchangeable, nor can the conclusions for one cohort be applied to the other.

In conclusion, in both a clinical registry and in cases undergoing clinical analysis, the rate of rejection of coronary CT angiography for fractional flow reserve derived from coronary CT angiography (FFR_{CT}) due to inadequate image quality is significantly lower than that reported in previous studies. Optimization of scans through heart rate control, timing of contrast material administration, minimization of section thickness and reconstructed field of view, and greater use of dual-source technology or a wide-coverage scanner holds the potential to enable FFR_{CT} analysis in most patients.

Author contributions: Guarantors of integrity of entire study, G.P., J.R.W.; 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, G.P., J.R.W., A.B., A.D.T., M.G., G.M., A.I.G., M.P., C.R., B.L.N., J.B., J.L.; clinical studies, G.P., J.R.W., A.B., G.M., A.I.G., D.A., M.P., K.N., T.A., C.R., B.L.N., G.L.R., K.C., T.F., L.H.K., J.L.; statistical analysis, G.P., J.R.W., L.F.; and manuscript editing, G.P., J.R.W., A.B., M.G., A.I.G., D.A., M.P., K.N., T.A., C.R., B.L.N., J.B., G.L.R., K.C., D.B., T.F., L.H.K., J.L.

Disclosures of Conflicts of Interest: **G.P.** Activities related to the present article: institution received a grant from HeartFlow. Activities not related to the present article: institution received grants from GE Healthcare, Bracco, and HeartFlow; institution received payment for lectures from GE Healthcare, Bracco, Bayer, and Medtronic. Other relationships: disclosed no relevant relationships. **J.R.W.** disclosed no relevant relationships. **A.B.** disclosed no relevant relationships. **A.D.T.** disclosed no relevant relationships. **L.F.** disclosed no relevant relationships. **M.G.** disclosed no relevant relationships. **G.M.** disclosed no relevant relationships. **A.I.G.** disclosed no relevant relationships. **D.A.** disclosed no relevant relationships. **M.P.** Activities related to the present article: institution received a grant from HeartFlow. Activities not related to the present article: institution served as a consultant for Bayer, Janssen, and AstraZeneca. Other relationships: disclosed no relevant relationships. **K.N.** Activities related to the present article: institution received a grant from HeartFlow. Activities not related to the present article: institution received grants from Siemens Healthineers, Bayer, and GE Healthcare; was reimbursed for travel by HeartFlow. Other relationships: disclosed no relevant relationships. **T.A.** Activities related to the present article: institution received grants from HeartFlow Japan; received a consulting fee and support for travel from HeartFlow Japan. Activities not related to the present article: is a consultant for Canon USA, Abbott Vascular Japan, Boston Scientific Japan, St Jude Medical Japan, and Terumo; received grants from Actelion Pharmaceuticals Japan, Acist Japan, Astellas Pharma, Bayer Japan, Boston Scientific Japan, Nippon Boehringer Ingelheim, Daiichi Sankyo, EP-CRSU, EPS, Goodman, Hearflow Japan, Infraredx, Kowa Pharmaceutical, MSD KK, Mebix, Mochida Pharmaceutical, Medtronic Japan, Novartis, Japan Lifeline, Nippon Shinyaku, Ono Pharmaceutical, Otsuka Pharmaceutical, Pfizer Japan, St. Jude Medical Japan, TOA EIYO, Takeda Pharmaceutical, Volcano Japan; served on speakers bureaus for Actelion Pharmaceuticals Japan, Acist Japan, Astellas Pharma, Amgen Astellas BioPharma, AstraZeneca, Abbott Vascular Japan, Nippon Boehringer Ingelheim, Bayer Japan, Bristol-Myers Squibb, Boston Scientific Japan, Canon Medical Systems, Chugai Pharmaceutical, Otsuka Pharmaceutical, Sumitomo Dainippon Pharma, Daiichi Sankyo, Eisai, Fujifilm, Goodman, HeartFlow Japan, Kyowa Hakko Kirin, Kowa Pharmaceutical, MSD KK, Nihon Medi-Physics, Mebix, Mochida Pharmaceutical, Medtronic Japan, Nipro, Novartis, Nippon Shinyaku, Philips Japan, St Jude Medical Japan, Sanofi, Shionogi & Company, Terumo, Toshiba Medical Systems, Takeda Pharmaceutical, and Volcano Japan; received travel assistance from TOA EIYO. Other relationships: disclosed no relevant relationships. **C.R.** Activities related to the present article: is an employee shareholder in HeartFlow. Activities not related to the present article: is a HeartFlow employee, holds stock in HeartFlow. Other relationships: disclosed no relevant relationships. **B.L.N.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: institution received grants from Siemens and HeartFlow; received travel aid from HeartFlow. Other relationships: disclosed no relevant relationships. **J.B.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: institution received grants from Edwards Lifesciences, GE Healthcare, Biotronik, Boston Scientific, and Medtronic; gave lectures for Abbott Vascular. Other relationships: disclosed no relevant relationships. **G.L.R.** Activities related to the present article: institution received a grant from HeartFlow. Activities not related to the present article: disclosed no relevant relationships. Other relationships: disclosed no relevant relationships. **K.C.** disclosed no relevant relationships. **D.B.** Activities related to the present article: institution received a grant from HeartFlow. Activities not related to the present article: receives royalties for software from Cedars-Sinai Medical Center. Other relationships: disclosed no relevant relationships. **T.F.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: is on the HeartFlow speakers bureau. Other relationships: disclosed no relevant relationships. **L.H.K.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: institution received grants from HeartFlow, Siemens Healthineers, and Verily; gave lectures for HeartFlow and Siemens Healthineers; developed educational presentations for Siemens and HeartFlow; received travel aid from GE Healthcare; other aid was received from Mallinckrodt. Other relationships: disclosed no relevant relationships. **J.L.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: is a consultant for HeartFlow and Circle Cardiovascular Imaging; institution received grants from Edwards Lifesciences, Abbott, and Medtronic; gave lectures for GE Healthcare; has stock in HeartFlow and Circle Cardiovascular Imaging; received travel aid from HeartFlow. Other relationships: disclosed no relevant relationships.

References

1. Lucas FL, DeLorenzo MA, Siewers AE, Wennberg DE. Temporal trends in the utilization of diagnostic testing and treatments for cardiovascular disease in the United States, 1993-2001. Circulation 2006;113(3):374–379.
2. Patel MR, Peterson ED, Dai D, et al. Low diagnostic yield of elective coronary angiography. N Engl J Med 2010;362(10):886–895.
3. Patel MB, Mor-Avi V, Kawaji K, et al. Role of Perfusion at Rest in the Diagnosis of Myocardial Infarction Using Vasodilator Stress Cardiovascular Magnetic Resonance. Am J Cardiol 2016;117(7):1072–1077.
4. Mowatt G, Cook JA, Hillis GS, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. Heart 2008;94(11):1386–1393.
5. Dewey M, Vavere AL, Arbab-Zadeh A, et al. Patient characteristics as predictors of image quality and diagnostic accuracy of MDCT compared with conventional coronary angiography for detecting coronary artery stenoses: CORE-64 Multicenter International Trial. AJR Am J Roentgenol 2010;194(1):93–102.
6. Pontone G, Bertella E, Mushtaq S, et al. Coronary artery disease: diagnostic accuracy of CT coronary angiography—a comparison of high and standard spatial resolution scanning. Radiology 2014;271(3):688–694.
7. Nørgaard 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.
8. 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 impacts study. Eur Heart J 2015;36(47):3359–3367.
9. Lu MT, Ferencik M, Roberts RS, et al. Noninvasive FFR Derived From Coronary CT Angiography: Management and Outcomes in the PROMISE Trial. JACC Cardiovasc Imaging 2017;10(11):1350–1358.
10. 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.
11. Nørgaard 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 Substudy of the NXT Trial. JACC Cardiovasc Imaging 2015;8(9):1045–1055.
12. Chinnaiyan KM, Akasaka T, Amano T, et al. Rationale, design and goals of the HeartFlow assessing diagnostic value of non-invasive FFR_{CT} in Coronary Care (ADVANCE) registry. J Cardiovasc Comput Tomogr 2017;11(1):62–67.
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(41):3701–3711.
14. Genders TS, Steyerberg EW, Alkadhi H, et al. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. Eur Heart J 2011;32(11):1316–1330.
15. 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):2233–2241.
16. Trattner S, Halliburton S, Thompson CM, et al. Cardiac-Specific Conversion Factors to Estimate Radiation Effective Dose From Dose-Length Product in Computed Tomography. JACC Cardiovasc Imaging 2018;11(1):64–74.
17. Achenbach S, Ropers U, Kuettner A, et al. Randomized comparison of 64-slice single- and dual-source computed tomography coronary angiography for the detection of coronary artery disease. JACC Cardiovasc Imaging 2008;1(2):177–186.
18. Weustink AC, Mollet NR, Neefjes LA, et al. Preserved diagnostic performance of dual-source CT coronary angiography with reduced radiation exposure and cancer risk. Radiology 2009;252(1):53–60.
19. Pontone G, Baggiano A, Andreini D, et al. Stress Computed Tomography Perfusion Versus Fractional Flow Reserve CT Derived in Suspected Coronary Artery Disease: The PERFECTION Study. JACC Cardiovasc Imaging 2018 Oct 12 [Epub ahead of print].
20. Pontone G, Baggiano A, Andreini D, et al. Diagnostic accuracy of simultaneous evaluation of coronary arteries and myocardial perfusion with single stress cardiac computed tomography acquisition compared to invasive coronary angiography plus invasive fractional flow reserve. Int J Cardiol 2018;273:263–268.
21. Korosoglou G, Marwan M, Giusca S, et al. Influence of irregular heart rhythm on radiation exposure, image quality and diagnostic impact of cardiac computed tomography angiography in 4,339 patients. Data from the German Cardiac Computed Tomography Registry. J Cardiovasc Comput Tomogr 2018;12(1):34–41.
22. Leipsic J, Abbara 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.
23. Abbara S, Blanke P, Maroules CD, et al. SCCT guidelines for the performance and acquisition of coronary computed tomographic angiography: A report of the society of Cardiovascular Computed Tomography Guidelines Committee: Endorsed by the North American Society for Cardiovascular Imaging (NASCI). J Cardiovasc Comput Tomogr 2016;10(6):435–449.
24. Chinnaiyan KM, Raff GL, Goraya T, et al. Coronary computed tomography angiography after stress testing: results from a multicenter, statewide registry, ACIC (Advanced Cardiovascular Imaging Consortium). J Am Coll Cardiol 2012;59(7):688–695.
25. Kanal KM, Stewart BK, Kolokythas O, Shuman WP. Impact of operator-selected image noise index and reconstruction slice thickness on patient radiation dose in 64-MDCT. AJR Am J Roentgenol 2007;189(1):219–225.