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

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

See also the editorial by Sakuma in this issue.

Background: Coronary artery fractional flow reserve (FFR) derived from CT angiography (FFR\textsubscript{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\textsubscript{CT}.

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

Materials and Methods: Prospectively acquired coronary CT angiography scans submitted as part of the Assessing Diagnostic Value of Noninvasive FFR\textsubscript{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\textsubscript{CT} rejection rate (defined as an inability to perform quantitative analysis with FFR\textsubscript{CT}). Factors that were associated with FFR\textsubscript{CT} rejection rate were assessed with multiple linear regression.

Results: In the ADVANCE registry, FFR\textsubscript{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\textsubscript{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\textsubscript{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.

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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 anatomic 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\textsubscript{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,
Determinants of Rejection Rate

Abbreviations

ADVANCE = Assessing Diagnostic Value of Noninvasive FFR\textsubscript{CT} in Coronary Care, CI = confidence interval, DICOM = Digital Imaging and Communications in Medicine, FFR = fractional flow reserve, FFR\textsubscript{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\textsubscript{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\textsubscript{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\textsubscript{CT} analysis could be performed in 87%–88% of coronary CT angiography data sets (7,8); however, a more recent sub-study 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\textsubscript{CT} analysis (9). Previous studies have examined the factors that affect the accuracy of FFR\textsubscript{CT} (for instance, both nitrate use and β-blocker use improve diagnostic accuracy) (10,11). However, factors that affect the ability to perform FFR\textsubscript{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\textsubscript{CT} analysis and the factors associated with an inability to perform FFR\textsubscript{CT} in the controlled Assessing Diagnostic Value of Noninvasive FFR\textsubscript{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\textsubscript{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\textsubscript{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\textsubscript{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\textsubscript{CT} analysis performed with version 2.0 or higher FFR\textsubscript{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\textsubscript{CT} analysis.—The decision to refer a patient for FFR\textsubscript{CT} analysis was made by the physician interpreting the coronary CT angiography images. All FFR\textsubscript{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 (FFRCT) analysis due to data format. Image quality rejection means image quality was inadequate to allow for generation of the anatomic coronary model necessary for FFRCT calculation. ADVANCE = Assessing Diagnostic Value of Noninvasive FFRCT in Coronary Care, CABG = coronary artery bypass graft, CTA = CT angiography, DICOM = Digital Imaging and Communications in Medicine.

End point.—Rate of coronary CT angiography rejection for FFRCT analysis was defined as the inability of technologists at HeartFlow, who were blinded to the clinical data, to perform FFRCT 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 FFRCT 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 FFRCT was not validated for clinical use and therefore was not suitable for analysis. This included a previous history of revascularization (sten 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 FFRCT 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 uninterpretable areas (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/m²)                       | 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 has typical symptoms                   | 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.
Patients in whom \( \text{FFR}_{\text{CT}} \) analysis was performed versus those who were rejected for \( \text{FFR}_{\text{CT}} \) analysis. Comparisons among groups of discrete variables were performed by using the \( \chi^2 \) 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 \( \text{FFR}_{\text{CT}} \) 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 10,621 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 (\( \leq 100 \text{ kVp} \)) 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 due to 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 \( \text{FFR}_{\text{CT}} \) analysis was greater in patients with a history of smoking, diabetes, or angina (Table 1). Technical factors associated with coronary CT angiography rejection for \( \text{FFR}_{\text{CT}} \) 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

#### Table 2: Baseline Characteristics of the Clinical Cohort

| Variable                              | All Patients (\( n = 10,416 \)) | \( \text{FFR}_{\text{CT}} \) Completed (\( n = 9,524 \)) | \( \text{FFR}_{\text{CT}} \) 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. \( \text{FFR}_{\text{CT}} \) = fractional flow reserve calculated from CT.
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 10,621 cases were submitted for FFR<sub>CT</sub> 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 10,416 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%]), Phillips (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 10,416 cases submitted (8.60%; 95% CI: 7.89%, 8.93%). Of the 10,416 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<sub>CT</sub> analysis showed a lower use of dual-source and wide-coverage CT scanners, lower aorta contrast, wider reconstructed fields of view, and a 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<sub>CT</sub> (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).

**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<sub>CT</sub>) analysis due to inadequate image quality is low, and it is lower in the Assessing Diagnostic Value of Noninvasive FFR<sub>CT</sub> 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<sub>CT</sub> analysis.

The observed rate of coronary CT angiography rejection for FFR<sub>CT</sub> 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...
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\textsubscript{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\textsubscript{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\textsubscript{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 4: Univariable Predictors of FFR\textsubscript{CT} Rejection in the ADVANCE Registry and Clinical Cohort |
| --- |
| Variable | ADVANCE Registry | Clinical Cohort |
| | 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/m\textsuperscript{2}) | 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) | .51 | 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 (1.0, 1.1) | .009 | 1.02 (1.01, 1.03) | <.001 |
| Dose (mSv) | 1.1 (1.0, 1.11) | .001 | 1.1 (1.09, 1.12) | <.001 |
| Heart rate (beats/min) | 1.0 (1.0, 1.1) | .001 | 1.1 (1.05, 1.06) | <.001 |
| Heart rate variability (beats/min) | 1.0 (0.99, 1.01) | .63 | 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\textsubscript{CT} in Coronary Care, FFR\textsubscript{CT} = fractional flow reserve calculated from CT.
Determinants of Rejection Rate

Table 5: Multivariable Predictors of FFR<sub>CT</sub> Rejection of the ADVANCE Registry and Clinical Cohort

| Variable                        | ADVANCE Registry | Clinical Cohort* |
|--------------------------------|------------------|------------------|
|                                | 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   | 1.0 (0.99, 1.00) | .11              | 0.997 (0.996, 0.998) | <.001          |
| Reconstructed field of view    | 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<sub>CT</sub> in Coronary Care, FFR<sub>CT</sub> = 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.

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<sub>CT</sub>. Thus, our study most likely represents the percentage of visually diagnostic coronary CT angiography scans amenable to subsequent FFR<sub>CT</sub> analysis rather than the percentage of all coronary CT angiography scans that are amenable to FFR<sub>CT</sub> 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<sub>CT</sub>) 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<sub>CT</sub> analysis in most patients.
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