Journal of Geriatric Cardiology | JGC
RESEARCH ARTICLE
J Geriatr Cardiol 2026; 23(1): 27–35

CT-derived fractional flow reserve combined with atherosclerotic extent to determine long-term outcomes in diabetic patients with coronary artery disease

Zhi-Qiang WANG, Zhen-Nan LI, Zhi-Hui HOU, Bin LU✉

Department of Radiology, Fuwai Hospital, State Key laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
✉ Correspondence to: lizhennan0827@163.com
https://doi.org/10.26599/1671-5411.2026.01.008

ABSTRACT

Background There is still limited data on predictive value of coronary computed tomography angiography (CCTA)–derived fractional flow reserve (CT-FFR) for long term outcomes. We examined the long-term prognostic value of CT-FFR combined with CCTA–defined atherosclerotic extent in diabetic patients with coronary artery disease (CAD).

Methods A retrospective pooled analysis of individual patient data was performed. Deep-learning-based vessel-specific CT-FFR was calculated. All patients enrolled were followed-up for at least 5 years. Predictive abilities for major adverse cardiac events (MACE) were compared among three models (model 1, constructed using clinical variables; model 2, model 1+CCTA–derived atherosclerotic extent (Leiden risk score); and model 3, model 2+CT-FFR.

Results A total of 480 diabetic patients [median age, 61 (55–66) years; 52.9% men] were included. During a median follow-up time of 2197 (2126–2355) days, 55 patients (11.5%) experienced MACE. In multivariate-adjusted Cox models, Leiden risk score (HR: 1.06; 95% CI: 1.01–1.11; $P = 0.013$) and CT-FFR ≤ 0.80 (HR: 6.54; 95% CI: 3.18–13.45; $P < 0.001$) were the independent predictors. The discriminant ability was higher in model 2 than in model 1 (C-index, 0.75 *vs.* 0.63; $P < 0.001$) and was further promoted by adding CT-FFR to model 3 (C-index, 0.81 *vs.* 0.75; $P = 0.002$). Net reclassification improvement (NRI) was 0.19 ($P = 0.009$) for model 2 beyond model 1. Of note, adding CT-FFR to model 3 also exhibited significantly improved reclassification compared with model 2 (NRI = 0.14; $P = 0.011$).

Conclusion In diabetic patients with CAD, CT-FFR provides robust and incremental prognostic information for predicting long-term outcomes. The combined model exhibits improved prediction abilities, which is beneficial for risk stratification.

In patients with diabetes, an even higher prevalence of coronary artery disease (CAD) has been noted.[1,2] The noninvasive coronary computed tomography angiography (CCTA) has been increasingly used to screen for CAD in diabetic patients with low to intermediate cardiovascular risk profile. The current practice guidelines emphasized the importance of cardiovascular risk assessment for this specific populations.[3] Previous studies have shown that the coronary atherosclerotic plaque extent, location and luminal stenosis detected by CCTA provide powerful prognostic information regarding the risk of cardiovascular events.[4–6] CCTA based risk scores such as Leiden risk score and CT Leaman score incorporating these prognostic information into a risk prediction model enable maximum use of the comprehensive anatomic interpretation of CCTA.[4] The Leiden risk score was shown to be a reliable cardiovascular risk predictor in diabetic patients with suspected CAD, and outperformed the Confirm score in predicting major adverse cardiovascular events (MACE).[7,8] Besides, Leiden risk score as well as the simplified CCTA-derived segment involvement score (SIS) were usually applied to quantify the atherosclerotic extent and were shown to be significantly associated with incremental risk of MACE in diabetic patients with non-obstructive CAD.[9] However, functional parameters were not included in these traditional prediction models, the noninvasive CCTA-derived fractional flow reserve (CT-FFR)

could play a pivotal role in clinical decision making and risk stratification. Except for anatomical information derived from CCTA, physiological evaluation by CT-FFR also provides significant prognostic value. Limited studies have exhibited the prognostic value of CT-FFR in diabetic cohort through short-medium term follow-up, which merits further validation across longer-term follow-up.[10–12]

Besides, with ongoing advancements in computer technologies, an on-site machine learning (ML) - based CT-FFR algorithm using an artificial intelligence (AI) platform has shown high diagnostic accuracy validated against invasive FFR, comparable with the off-site computational fluid dynamics based algorithms. Similarly, with development of AI technologies, newly developed deep learning (DL) based CT-FFR has also shown its powerful diagnostic performance and prognostic value at medium-term follow-up.[13–15] The AI assisted CT-FFR technique incorporating CCTA has become a highly promising tool for risk prediction. We hypothesize that combining the DL-based vessel-specific CT-FFR with CCTA defined atherosclerotic extent can provide incremental prognostic value for diabetic patients with CAD. The purpose of the present study was to investigate the impact of the functional CT-FFR combined with atherosclerotic extent on long-term outcomes in diabetic patients with CAD.

METHODS

Patients

This single-center retrospective cohort study was performed at Fuwai Hospital in China, complied with the tenets of the Declaration of Helsinki, and was approved by the ethics review board of the Fuwai Hospital. The requirement for informed consent was waived. Consecutive type 2 diabetic patients who were clinically suspected (but without known) of having stable CAD and were accordingly referred for their first CCTA from February 2017 through July 2018 were candidates for inclusion in our study. We included subjects (1) age ≥ 18 years, (2) with at least one atherosclerotic lesion on CCTA images with a luminal diameter < 90% in a vessel segment of 2 mm or greater, and (3) with outpatient or inpatient electronic medical records in our hospital. We excluded those (1) with poor image quality for CT-FFR and plaque analysis (significant motion artifacts or poor contrast enhancement), (2) with revascularization driven by CCTA results within 3 months, and (3) with incomplete clinical data or who were lost to clinical follow-up.

CCTA Protocol and Interpretation

All image acquisitions were performed using CT scanners with at least 64 detector rows, including dual-source (Somatom Definition Flash, Siemens Healthineers), 256-section wide-detector (Revolution CT, GE Healthcare), and 320-detector row (Aquilion One, Canon Corporation) CT scanners. Scan parameters were set according to the Society of Cardiovascular Computed Tomography guidelines.[16] β-blockers were administered by their treating physicians if necessary. Prospective electrocardiographic gating was used for all scans.

All the CT images acquired at the time of diagnosis were used for analysis. All the raw data of the scans were transferred to a workstation (Vitrea fX, version 3.0; Canon Medical Systems) for three-dimensional image reconstruction. Two experienced observers who were blinded to all patient characteristics and the clinical outcomes analyzed the coronary vessels independently. Disagreements were resolved by consensus or by adjudication from a third senior expert. The type and location of the lesion were visually evaluated based on the 17-segment modified American Heart Association classification. Plaque composition was classified as noncalcified plaque (having lower density than the contrast-enhanced lumen), calcified plaque (with high density), and mixed plaque (both noncalcified and calcified elements existed).[8] The presence of coronary stenosis was visually assessed in all vessels of at least 2-mm diameter, with stenosis severity dichotomized as anatomically obstructive or non-obstructive, defined as ≥ 50% degree of stenosis or < 50% degree of stenosis, respectively. The comprehensive Leiden risk score was calculated and further stratified into low-risk (< 5), moderate-risk (5–20), and high-risk (> 20) groups, as previously described, which integrated the plaque composition and the degree of stenosis with the location of the coronary plaque to reflect the coronary atherosclerotic burden.[4,7,8] The segment involvement score (SIS) was also calculated to quantify the atherosclerosis extent. It was calculated as the total number of coronary artery segments that exhibits plaque without consideration of stenosis (ranging from 0 to 16), and further subdivided into SIS < 3 and SIS ≥ 3.[9,11]

Evaluation of Deep Learning (DL)-Based CT-FFR

Deep learning–based CT-FFR calculations were retrospectively performed on a CT-FFR workstation (DEEPVESSEL FFR, Keya Medical Technology Co., Ltd., Beijing, China) by experts blinded to coronary CT angiography findings and clinical outcomes without affecting clinical management. Treating physicians were blinded to the results of CT-FFR. Hence, CT-FFR results did not influence clinical decision-making. Invasive coronary angiography and revascularization decisions were made at the discretion of treating physicians. The vessel-specific CT-FFR value was obtained directly as the output, and the threshold value of CT-FFR ≤ 0.80 was regarded as hemodynamically significant. The lowest vessel-specific CT-FFR value detected from the whole coronary tree was used for per-patient level analysis. The details of the DEEPVESSEL FFR algorithm, diagnostic performance, and concordance of the DEEPVESSEL FFR with invasive FFR have been reported previously.[13–15]

Clinical Data Collection and Follow-up

Baseline clinical data about patient characteristics and clinical course were obtained retrospectively from the medical records. Relevant patient information included patient age, sex, cardiovascular risk factors, and therapeutic regimen. Follow-up data (survival information, cause of death, and interventions) were collected through clinical visits or telephone contact with the patients or their relatives. All reported events were verified by reviewing hospital records or contact with the attending physicians. The primary outcome of interest was MACE, defined as composite outcomes of cardiac death, nonfatal myocardial infarction, unstable angina requiring hospitalization, and late revascularization (occurred 3 months after index CCTA). All enrolled patients were followed up for at least 5 years or until the occurrence of the earliest outcome.

Statistical Analysis

Statistical analysis was performed using the SPSS statistical package (version 26.0, IBM, Armonk, New York, USA), the R statistical package (version 4.3.3), and Python (version 3.10.14). Continuous variables were expressed as median (interquartile range), and categorical variables were expressed as absolute numbers and percentages. Continuous variables that were non-normally distributed variables were compared using the Mann–Whitney *U* test. The chi-squared test or Fisher's exact test, as appropriate, was used for categorical variables. Cumulative incidence rates of the outcomes were estimated using the Kaplan–Meier method and compared with the log-rank test between different groups. The Cox proportional hazards model was used to identify factors associated with the development of the MACE. Variables with statistical significance set at $P < 0.10$ (two-sided) in univariate analysis were included in the multivariate analysis and used for constructing prediction models. The base prediction model (model 1) was built using baseline clinical variables, and a further prediction model (model 2) was constructed based on model 1 and the CCTA defined comprehensive atherosclerotic extent (Leiden risk score). Moreover, to investigate the incremental prognostic value of CT-FFR, a combined prediction model (model 3) was constructed by overlaying CT-FFR on top of model 2. The predictive abilities of these models were investigated and compared using Harrell's C-statistics (C-index), time-dependent ROC curve analysis, net reclassification improvement (NRI), and integrated discrimination improvement (IDI). All *P* values were two-sided, with a *P* value < 0.05 considered statistically significant.

RESULTS

Baseline Characteristics and Clinical Outcomes

A total of 685 diabetic patients with suspected CAD underwent CCTA at baseline, among which 539 patients were detected as having coronary stenoses, and 59 patients were excluded because of pre-specified criteria (Figure 1). Consequently, the final cohort consisted of 480 patients. Of these patients, 254 (52.9%) were men and 226 (47.1%) were women, with a median age of 61 (55–66) years. The median age of the male patients was lower than that of the female patients [59 (53–65) *vs.* 63 (59–68) years; $P < 0.001$]. As for CT characteristics, 138 (28.7%) patients were detected as having obstructive CAD, the median Leiden risk score and segment involvement score were 7.50 (4.55–11.25) and 3 (2–4), respectively. Median CT-FFR of the full cohort was 0.83 (0.79–0.85), with 140 (29.2%) patients had CT-FFR ≤ 0.80.

During a median follow-up time of 2197 (2126–2355) days, 55 patients (11.5%) experienced MACE, including 1 cardiac deaths, 13 nonfatal myocardial infarctions, 17 unstable angina requiring hospitalization, and 24 late re-

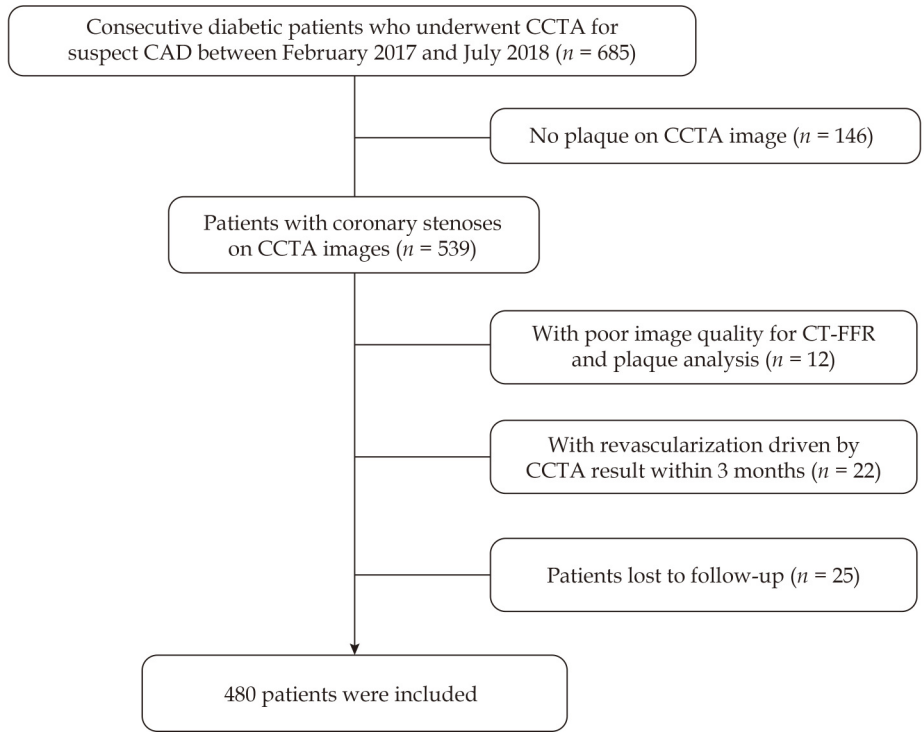

Figure 1 Flowchart of the study population. CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CT-FFR: CCTA-derived fractional flow reserve.

vascularization (occurred 3 months after index CCTA). The incidence of outcomes was more frequent in male than female patients (14.6% *vs.* 8.0%; $P = 0.023$). Patients with MACE had higher prevalence of ever smokers (60.0% *vs.* 37.4%; $P = 0.001$), ever drinkers (61.8% *vs.* 44.5%; $P = 0.015$), history of stroke (20.0% *vs.* 11.8%; $P = 0.084$), obstructive CAD (72.7% *vs.* 23.1%; $P < 0.001$), SIS ≥ 3 (72.7% *vs.* 48.2%; $P = 0.001$), CT-FFR ≤ 0.80 (78.2% *vs.* 22.8%; $P < 0.001$), and higher Leiden risk score [12.65 (8.42–18.06) *vs.* 7.15 (4.20–10.48); $P < 0.001$], as well as higher SIS [4 (2–7) *vs.* 2 (2–4); $P < 0.001$], compared with those without MACE. Clinical and CT characteristics of the full cohort and comparisons between patients with and without outcomes are presented in Table 1. Figure 2 depicted Kaplan-Meier curves for cumulative event rate of MACE according to obstructive CAD, Leiden risk score, SIS and CT-FFR. Significantly higher event rates were observed in patients with obstructive CAD, higher Leiden risk score and SIS group, as well as CT-FFR ≤ 0.80.

Cox regression Analysis for Predicting MACE

Cox regression analysis comprehensively investigated predictors associated with the outcomes. In the univariate analysis, male (HR: 1.90; 95% CI: 1.08–3.34; $P = 0.026$), ever smokers (HR: 2.34; 95% CI: 1.37–4.02; $P = 0.002$), ever drinkers (HR: 1.89; 95% CI: 1.10–3.26; $P = 0.022$), history of stroke (HR: 1.86; 95% CI: 0.96–3.59; $P = 0.067$), Leiden risk score (HR: 1.13; 95% CI: 1.09–1.17; $P < 0.001$), and CT-FFR ≤ 0.80 (HR: 10.40; 95% CI: 5.48–19.74; $P < 0.001$) were all predictors for the outcomes, which were subsequently included into further multivariate Cox regression analysis for development of prediction models. Table 2 summarized findings of the nested multivariate-adjusted Cox models.

Development and Comparison of Prediction Models

In the base model (model 1) constructed using baseline clinical variables, ever smokers (HR: 2.45; 95% CI: 1.04–5.78; $P = 0.040$) and history of stroke (HR: 2.20; 95% CI: 1.13–4.31; $P = 0.021$) was the independent predictors for outcomes. In the further built prediction model (model 2) based on model 1 and Leiden risk score, after adjustment, history of stroke (HR: 2.15; 95% CI: 1.10–4.22; $P = 0.026$) and Leiden risk score (HR: 1.13; 95% CI: 1.08–1.17; $P < 0.001$) remained the independent predictors for outcomes. In the combined prediction model (model 3) constructed by overlaying CT-FFR on top of the model 2, after adjustment, Leiden risk score (HR:

Table 1 Characteristics of study cohort by outcome.

Parameter	Full cohort (*n* = 480)	MACE		*P*-value
		Yes (*n* = 55)	No (*n* = 425)	
Age, yrs	61 (55–66)	61 (55–67)	61 (55–66)	0.988
Male	254 (52.9%)	37 (67.3%)	217 (51.1%)	0.023
Hypertension	308 (64.2%)	38 (69.1%)	270 (63.5%)	0.418
Dyslipidemia	292 (60.8%)	33 (60.0%)	259 (60.9%)	0.893
Ever smokers*	192 (40.0%)	33 (60.0%)	159 (37.4%)	0.001
Ever drinkers	223 (46.5%)	34 (61.8%)	189 (44.5%)	0.015
Family history of CAD	112 (23.3%)	12 (21.8%)	100 (23.5%)	0.778
History of stroke	61 (12.7%)	11 (20.0%)	50 (11.8%)	0.084
History of PVD	100 (20.8%)	14 (25.5%)	86 (20.2%)	0.370
Obstructive CAD	138 (28.7%)	40 (72.7%)	98 (23.1%)	< 0.001
Single vessel	102 (21.3%)	26 (47.3%)	76 (17.9%)	< 0.001
Two vessel	23 (4.8%)	9 (16.4%)	14 (3.3%)	< 0.001
Three vessel	13 (2.7%)	5 (9.1%)	8 (1.9%)	0.010
Leiden risk score	7.50 (4.55–11.25)	12.65 (8.42–18.06)	7.15 (4.20–10.48)	< 0.001
< 5	142 (29.6)	6 (10.9)	136 (32.0)	0.001
5-20	318 (66.3)	41 (74.5)	277 (65.2)	0.167
> 20	20 (4.2)	8 (14.5)	12 (2.8)	0.001
SIS	3 (2–4)	4 (2–7)	2 (2–4)	< 0.001
SIS ≥ 3	245 (51.0)	40 (72.7)	205 (48.2)	0.001
CT-FFR	0.83 (0.79–0.85)	0.78 (0.75–0.80)	0.83 (0.81–0.85)	< 0.001
CT-FFR ≤ 0.80	140 (29.2%)	43 (78.2%)	97 (22.8%)	< 0.001

Values are median (interquartile range) or *n* (%). *Smoking, ever; current smokers and former smokers. CAD: coronary artery disease; CT-FFR: CT - derived fractional flow reserve; MACE: major adverse cardiac events; PVD: Peripheral vascular disease; SIS: Segment Involvement Score.

1.06; 95% CI: 1.01–1.11; $P = 0.013$) and CT-FFR ≤ 0.80 (HR: 6.54; 95% CI: 3.18–13.45; $P < 0.001$) were still the independent predictors. ROC curves for different models in predicting outcomes were shown in Figure 3.

We investigated and compared predictive performance of the established models by C-index, time-dependent AUC, NRI, IDI, as shown in Table 3. The discriminant ability in predicting outcomes was higher in model 2 than in model 1 (C-index, 0.75 *vs.* 0.63; $P < 0.001$) and was further promoted by adding CT-FFR to model 3 (C-index, 0.81 *vs.* 0.75; $P = 0.002$). Time-dependent ROC curve analysis revealed similar trends across 3-year and 5-year area under the ROC curve (AUC). NRI was 0.19 ($P = 0.009$) for model 2 beyond model 1 with the addition of Leiden risk score. Of note, adding CT-FFR to model 3 also exhibited significantly improved reclassification compared with model 2 (NRI = 0.14; $P = 0.011$), as were similar results in IDI analysis.

DISCUSSION

In this retrospective pooled analysis of a Chinese cohort with concomitant diabetes and CAD, we investigated the additional prognostic value of the DL-based vessel-specific CT-FFR beyond the CCTA defined atherosclerotic extent and traditional cardiovascular risk factors, and proposed simplified prediction models for long-term outcomes. Briefly, we found that CT-FFR provided incremental prognostic information for long-term outcomes in diabetic patients with CAD. Combined models including clinical and CT-derived atherosclerotic extent and functional CT-FFR allow for accurate estimation of the risk of clinical outcomes. The proposed predictive model is helpful for risk stratification for diabetic patients with CAD.

There have been limited researches addressing the potential prognostic value of CT-FFR in the diabetes population, which confirmed CT-FFR as a strong independ-

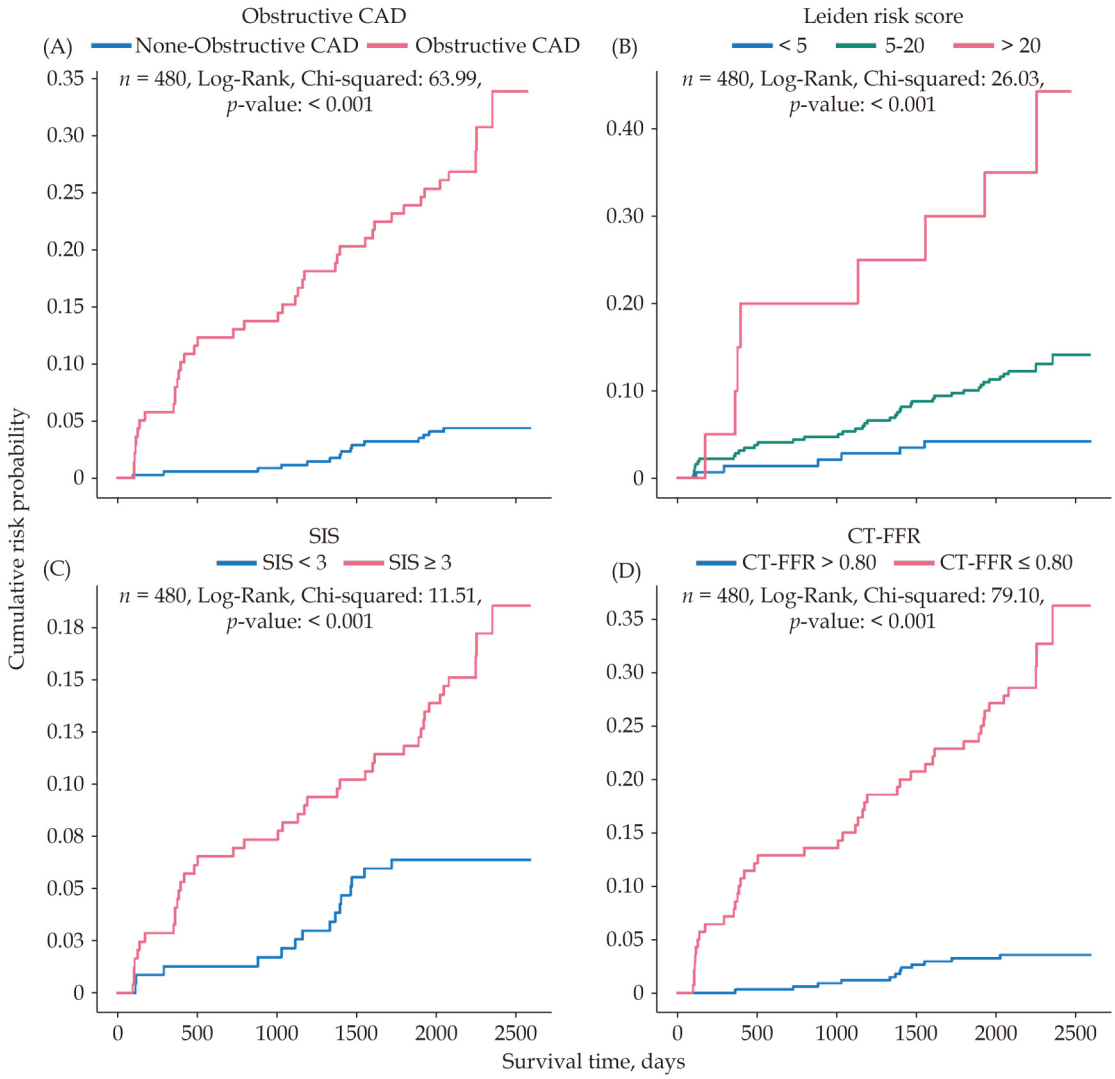

Figure 2 Kaplan–Meier Curves for the Cumulative Event Rate of MACE according to obstructive CAD (A), Leiden risk score (B), SIS (C) and CT-FFR (D). CAD: coronary artery disease; CT-FFR: coronary computed tomography angiography-derived fractional flow reserve; MACE: major adverse cardiovascular event; SIS: segment involvement score.

ent predictor for MACE through short-medium term follow-up,[10–12] however, there is still a lack of study to investigate the impact of CT-FFR on long-term outcomes. Besides, CT-FFR in previous studies was measured by different technologies, which might lead to some discrepancies between different studies. For example, in a retrospective cohort study, functional assessment by myocardial perfusion imaging but not CT-FFR added independent and incremental prognostic information to CCTA based anatomical assessment and clinical risk factors in predicting incident outcomes.[17] In the present study, we used the DL-based vessel-specific CT-FFR method, this on-site algorithm exhibited robust diagnostic performance and prognostic value even in the setting of extensive coronary artery calcium,[18] comparable with the off-site computational fluid dynamics–based algorithms. Consistent with previous findings, we further demonstrated the favorable predictive value of CT-FFR in the diabetes population across longer-term follow-up, suggesting its great potential in clinical practice for risk stratification and decision-making for diabetic patients.

Coronary artery disease in diabetics is associated with more diffuse atherosclerosis and increased plaque burden, that are more susceptible to unfavorable clinical outcomes.[1,2,9] CCTA is increasingly used in clinical practice as a noninvasive imaging tool for detection of CAD in diabetic population, which can provide abundant

Table 2 Cox Regression Analysis and predictive models for MACE.

Parameters	MACE							
	Univariate analysis		Model 1		Model 2		Model 3	
	HR (95% CI)	*P*-value	HR (95% CI)	*P* value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age, yrs	1.01 (0.98–1.04)	0.552						
Male	1.90 (1.08–3.34)	0.026	1.00 (0.41–2.40)	0.991	0.74 (0.31–1.78)	0.500	0.65 (0.28–1.51)	0.314
Hypertension	1.29 (0.73–2.28)	0.388						
Dyslipidemia	0.98 (0.57–1.68)	0.938						
Ever smokers	2.34 (1.37–4.02)	0.002	2.45 (1.04–5.78)	0.040	2.26 (0.94–5.43)	0.067	2.02 (0.84–4.89)	0.117
Ever drinkers	1.89 (1.10–3.26)	0.022	1.05 (0.45–2.48)	0.905	1.21 (0.49–2.96)	0.678	1.20 (0.51–2.84)	0.677
Family history of CAD	0.89 (0.47–1.69)	0.727						
History of stroke	1.86 (0.96–3.59)	0.067	2.20 (1.13–4.31)	0.021	2.15 (1.10–4.22)	0.026	1.89 (0.95–3.75)	0.071
History of PVD	1.43 (0.78–2.64)	0.248						
Leiden risk score	1.13 (1.09–1.17)	< 0.001			1.13 (1.08–1.17)	< 0.001	1.06 (1.01–1.11)	0.013
< 5	1							
5–20	3.15 (1.34–7.42)	0.009						
> 20	11.38 (3.95–32.81)	< 0.001						
CT-FFR ≤ 0.80	10.40 (5.48–19.74)	< 0.001					6.54 (3.18–13.45)	< 0.001

CAD: coronary artery disease; CT-FFR: CT - derived fractional flow reserve; MACE: major adverse cardiac events; PVD: Peripheral vascular disease; SIS: Segment Involvement Score.

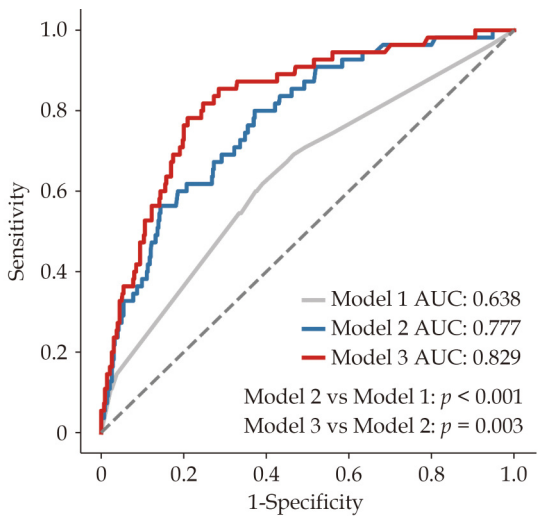

Figure 3 ROC curves for different models in predicting MACE. CT-FFR: coronary computed tomography angiography-derived fractional flow reserve; MACE: major adverse cardiovascular event; ROC curve: receiver operating characteristic curve; SIS: segment involvement score. Model 1 was built using baseline clinical variables, model 2 was constructed based on model 1 and the CCTA defined atherosclerotic extent (Leiden risk score), model 3 was constructed by overlaying CT-FFR on top of model 2.

anatomical information including luminal stenosis severity, plaque burden, high-risk plaques, and coronary calcium scores. In recent years, some CCTA-derived scoring systems have been developed and exhibited promising utility in risk stratification, such as Leiden risk score and segment involvement score.[4] Previous studies have confirmed their significant prognostic value in diabetic patients with suspected CAD, and their advantages over traditional risk scores, such as the Coronary Artery Disease Reporting and Data System score based on stenosis severity only, and Confirm Score.[7] The Leiden risk score was considered as an effective and reliable method for quantifying atherosclerotic extent, which was reported more strongly predictive than the segment involvement score.[9] In the present study, we chose the Leiden risk score as a simplified comprehensive anatomical interpretation of CCTA, and further confirmed the long-term prognostic value of it in diabetic patients with CAD, indicated that atherosclerotic extent detected by CCTA has great potential in clinical practice for risk estimates. However, functional parameters were not included in these traditional scores. We further developed a combined model to investigate the additional prognostic value of the functional CT-FFR by overlaying CT-FFR on top of the CCTA defined atherosclerotic extent. Our results strongly emphasized the independent and incremental predictive value of CT-FFR beyond CCTA defined atherosclerotic extent and clinical risk factors. The new combined prediction model incorporating CT-FFR may be well applied to tailor medical treatment to the diabetic patient by identifying who are truly suitable for higher-intensity medical therapies and need extens-

Table 3 Predictive performance and comparison of discriminant ability of the models.

Models	C-index (95%CI)	*P*-value	Time-dependent AUC		NRI	*P*-value	IDI	*P*-value
			3-year	5-year				
Model 1 (Base Model)	0.63 (0.57–0.72)		0.66	0.63				
Model 2: Model 1 + Leiden score	0.75 (0.70–0.81)	$P < 0.001$ *vs* Model 1	0.78	0.75	0.19	$P = 0.009$ *vs* Model 1	0.09	$P < 0.001$ *vs* Model 1
Model 3: Model 2 + CT-FFR	0.81 (0.77-0.86)	$P = 0.002$ *vs* Model 2	0.83	0.80	0.14	$P = 0.011$ *vs* Model 2	0.06	$P < 0.001$ *vs* Model 2

C-index: Harrell's C-statistics; IDI: integrated discrimination improvement; NRI: net reclassification improvement.

ive follow-up for prognostic reasons. Future researches should investigate whether clinical outcomes can be improved by the application of this simplified predictive model allowing for personalized risk assessment and medical therapy.

Study Limitation

There were several limitations in the present study. First, this study was not free from selection bias due to the single-center retrospective design, which may somewhat affect the accuracy of the proposed predictive model. Whether the predictive value of the model can be largely translated into practical clinical utility remains to be further verified in larger, prospective, multicenter investigations. Second, sophisticated plaque characterization analysis, such as high-risk plaque features, was not systematically assessed in this study, which also provided important prognostic information.[19,20] However, sophisticated plaque characterization analysis relies on software applications, and the accuracy of measurement can be compromised by extensive or severe calcification and discrepancies among different software and observers. It has not been extensively used in our routine clinical practice. We sought to propose a relatively simple and practical model for risk stratification and chose the comprehensive Leiden risk score with a combination of anatomy and simplified plaque characterization. Third, downstream medication treatments and lifestyle modification were not included in the multivariate analysis, which may lead to potential confounders. Besides, we focused on the diabetic population with coronary atherosclerosis, the diabetes duration and treatment information during follow-up were not clear, which can also impact on the long-term clinical outcomes.

Conclusion

In diabetic patients with CAD, the DL-based vessel-specific CT-FFR provides independent and additional prognostic value for long-term outcomes compared with the CCTA defined atherosclerotic extent and traditional cardiovascular risk factors. Diabetic patients with greater atherosclerotic extent and CT-FFR ≤ 0.80 are more likely to experience unfavorable long-term outcomes, which, to a large extent, means the need for subsequent higher-intensity therapies and extensive follow-up for prognostic reasons. The proposed models are helpful for risk stratification and decision-making.

REFERENCES

[1] Kim U, Leipsic JA, Sellers SL, *et al.* Natural History of Diabetic Coronary Atherosclerosis by Quantitative Measurement of Serial Coronary Computed Tomographic Angiography: Results of the PARADIGM Study. *JACC Cardiovasc Imaging* 2018; 11: 1461–1471.

[2] Park GM, Lee JH, Lee SW, *et al.* Comparison of coronary computed tomographic angiographic findings in asymptomatic subjects with versus without diabetes mellitus. *Am J Cardiol* 2015; 116: 372–378.

[3] Cosentino F, Grant PJ, Aboyans V, *et al.* 2019 ESC guidelines on diabetes, prediabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J* 2020; 41: 255–323.

[4] Serruys PW, Hara H, Garg S, *et al.* Coronary computed tomographic angiography for complete assessment of coronary artery disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2021; 78: 713–736.

[5] van Rosendael AR, Bax AM, Smit JM, *et al.* Clinical risk factors and atherosclerotic plaque extent to define risk for major events in patients without obstructive coronary artery disease: the long-term coronary computed tomography angiography CONFIRM registry. *Eur Heart J Cardiovasc Imaging* 2020; 21: 479–488.

[6] Han D, Chen B, Gransar H, *et al.* Prognostic significance of plaque location in non-obstructive coronary artery disease: from the CONFIRM registry. *Eur Heart J Cardiovasc Imaging* 2022; 23: 1240–1247.

[7] Liu Z, Ding Y, Dou G, *et al.* CT-based leiden score outperforms confirm score in predicting major adverse cardiovascular events for diabetic patients with suspected coronary artery disease. *Korean J Radiol* 2022; 23: 939–948.

[8] van Rosendael AR, Shaw LJ, Xie JX, *et al*. Superior risk stratification with coronary computed tomography angiography using a comprehensive atherosclerotic risk score. *J Am Coll Cardiol Img* 2019; 12: 1987–1997.
[9] Ding Y, Liu Z, Dou G, *et al*. Prognostic value of atherosclerotic extent in diabetic patients with nonobstructive coronary artery disease. *J Diabetes Res* 2021; 2021: 5597467.
[10] Lan Z, Ding X, Yu Y, *et al*. CT-derived fractional flow reserve for prediction of major adverse cardiovascular events in diabetic patients. *Cardiovasc Diabetol* 2023; 22: 65.
[11] Liu Z, Ding Y, Dou G, *et al*. Global trans-lesional computed tomography-derived fractional flow reserve gradient is associated with clinical outcomes in diabetic patients with non-obstructive coronary artery disease. *Cardiovasc Diabetol* 2023; 22: 186.
[12] Gulsin GS, Tzimas G, Holmes KR, *et al*. Impact of coronary CT angiography-derived fractional flow reserve on downstream management and clinical outcomes in individuals with and without diabetes. *Radiol Cardiothorac Imaging* 2023; 5: e220276.
[13] Yang J, Shan D, Wang X, *et al*. On-site computed tomography–derived fractional flow reserve to guide management of patients with stable coronary artery disease: the TARGET randomized trial. *Circulation* 2023; 147: 1369–1381.
[14] Liu X, Mo X, Zhang H, *et al*. A 2-year investigation of the impact of the computed tomography–derived fractional flow reserve calculated using a deep learning algorithm on routine decision-making for coronary artery disease management. *Eur Radiol* 2021; 31: 7039–7046.
[15] Wang ZQ, Zhou YJ, Zhao YX, *et al*. Diagnostic accuracy of a deep learning approach to calculate FFR from coronary CT angiography. *J Geriatr Cardiol* 2019; 16: 42–48.
[16] 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: 435–449.
[17] Ahmed AI, Han Y, Al Rifai M, *et al*. Prognostic Value of Computed Tomography-Derived Fractional Flow Reserve Comparison With Myocardial Perfusion Imaging. *JACC Cardiovasc Imaging* 2022; 15: 284–295.
[18] Dey D, Lin A. Machine-Learning CT-FFR and Extensive Coronary Calcium: Overcoming the Achilles Heel of Coronary Computed Tomography Angiography. *JACC Cardiovasc Imaging* 2020; 13: 771–773.
[19] Sato Y, Motoyama S, Miyajima K, *et al*. Clinical outcomes based on coronary computed tomography-derived fractional flow reserve and plaque characterization. *JACC Cardiovasc Imaging* 2024; 17: 284–297.
[20] Nurmohamed NS, van Rosendael AR, Danad I, *et al*. Atherosclerosis evaluation and cardiovascular risk estimation using coronary computed tomography angiography. *Eur Heart J* 2024; 45: 1783–1800.

Please cite this article as: WANG ZQ, LI ZN, HOU ZH, LU B. CT-derived fractional flow reserve combined with atherosclerotic extent to determine long-term outcomes in diabetic patients with coronary artery disease. *J Geriatr Cardiol* 2026; 23(1): 27–35. DOI: 10.26599/1671-5411.2026.01.008