METHODIST DEBAKEY CARDIOVASCULAR JOURNAL

Artificial Intelligence in Coronary Artery Disease: From Detection to Precision Management

REVIEW

KESHAV GARG, MD
LANDON BRUICH, MD
LUKE J. ENEMARK, BA
KHALID SAWALHA, MD
AAKASH RANA, MD
ANKIT AGRAWAL, MD
ROBERT F. SPRAGGINS II, MD
OSAMA KHALAILA, MD
MOHANAD SHEHADEH, MD
BUTHAINAH ALHWARAT, MD
CARSTEN JOHNSON, BS
AVIRUP GUHA, MD, MPH
YIYE ZHANG, MS, PHD
GIANLUCA PONTONE, MD, PHD
SOURBHA S. DANI, MD, MSC
VIGNESH CHINDAMBARAM, MD, MPH
LOHENDRAN BASKARAN, MBBS
BHUPENDAR TAYAL, MD, PHD
SUBHI J. AL'AREF, MD

*Author affiliations can be found in the back matter of this article

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

CORRESPONDING AUTHOR:
Subhi J. Al'Aref, MD
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US
SJAlaref@uams.edu

ABSTRACT

Coronary artery disease (CAD) remains the leading cause of death worldwide, yet the landscape is rapidly evolving as artificial intelligence (AI) is increasingly applied to its detection, diagnosis, and management. This review surveys the expanding role of AI across the full spectrum of CAD care. In screening, deep-learning electrocardiography and electronic health record-based digital markers enable earlier identification of clinically significant disease. In noninvasive imaging, AI-driven coronary computed tomography angiography automates calcium scoring, derives fractional flow reserve without invasive wires, and quantifies high-risk plaque features that predict incident adverse events. Within the cardiac catheterization laboratory, angiography-derived physiologic assessment and AI-guided intravascular imaging segmentation support real-time procedural decision-making. Beyond diagnosis, machine-learning models integrating multimodality imaging data improve risk stratification over conventional clinical scores, while pharmacogenomic algorithms and wearable-based digital rehabilitation platforms enable patient-centric secondary prevention. Despite this progress, significant challenges persist, including limited evidence from randomized trials, algorithmic bias in underrepresented populations, regulatory uncertainty surrounding software-as-a-medical-device frameworks, and the risk of clinician de-skilling. AI has the potential to act as a collaborative tool that augments—rather than replaces—physician judgment. Future directions include foundation models, multiomics integration, agentic AI workflows, and equity-centered deployment strategies to ensure that AI-driven advances benefit all individuals with CAD.

KEYWORDS:
artificial intelligence; coronary artery disease; machine learning; deep learning; coronary computed tomography angiography; fractional flow reserve; risk stratification; precision medicine

TO CITE THIS ARTICLE:
Garg K, Bruich L, Enemark LJ, Sawalha K, Rana A, Agrawal A, Spraggins II RF, Khalaila O, Shehadeh M, Alhwarat B, Johnson C, Guha A, Zhang Y, Pontone G, Dani SS, Chindambaram V, Baskaran L, Tayal B, Al'Aref SJ. Artificial Intelligence in Coronary Artery Disease: From Detection to Precision Management. Methodist DeBakey Cardiovasc J. 2026;22(5):20-38. doi: 10.14797/mdcvj.1917

INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of death globally and in the United States (US), accounting for ~9.44 million deaths worldwide annually.[1] Global CAD prevalence continues to rise with population growth and aging, and low- to middle-income countries bear a disproportionate share of the burden. The Prospective Urban Rural Epidemiology study demonstrated that despite fewer cardiovascular risk factors, low-income countries experience 4-fold higher cardiovascular mortality than high-income countries, largely due to limited diagnostic and treatment access.[2] In the US, persistent racial and socioeconomic disparities in CAD outcomes underscore the need for more equitable diagnostic and management strategies.[3] These gaps highlight the potential of artificial intelligence (AI) to expand access to early detection, accurate diagnosis, and individualized CAD management.

For instance, AI enables earlier detection of subclinical atherosclerosis, provides novel noninvasive cardiac imaging insights, assists with cardiac catheterization laboratory (CCL) procedural guidance, and supports individualized management strategies. The emerging paradigm envisions AI as a continuous collaborative partner, enabling real-time tracking of disease development and creating opportunities for timely intervention before irreversible damage occurs.[4] This review synthesizes current evidence for AI applications across the CAD care continuum: screening and early detection, noninvasive diagnostic imaging, invasive assessment and procedural guidance, risk stratification and prognostication, precision therapeutics and secondary prevention, and cross-cutting challenges and future directions that will determine clinical adoption (Figure 1).[5]

A structured literature search was conducted across PubMed, Embase, and IEEE Xplore through June 2026 using terms combining artificial intelligence, machine learning, and deep learning with coronary artery disease and its diagnostic and therapeutic subdomains. Priority was given to randomized trials, large registries, meta-analyses, and society statements; selected single-center studies were included when they represented novel applications without higher-level evidence.

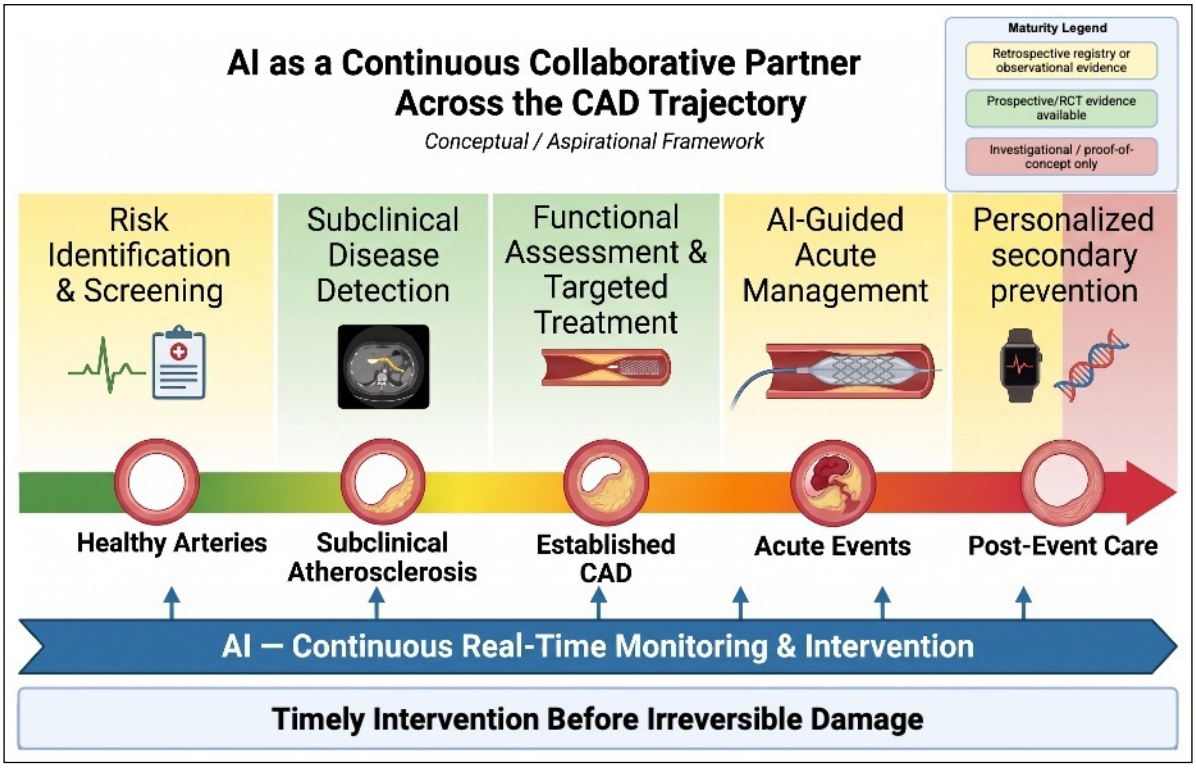


Figure 1 AI as a continuous collaborative partner across the CAD trajectory. A five-stage framework illustrates how AI intercepts disease progression at each phase: from risk identification and screening in healthy individuals, through subclinical disease detection, functional assessment and targeted treatment in established CAD, AI-guided acute management, to personalized secondary prevention, enabling timely intervention before irreversible damage occurs. A color-coded maturity legend indicates the current evidence level for each stage: yellow (retrospective registry or observational evidence), green (prospective/RCT evidence available), and red (investigational/proof-of-concept only). This framework is conceptual and aspirational; continuous real-time AI monitoring across all stages has not yet been clinically validated. Originally created with BioRender.com.[5] AI: artificial intelligence; CAD: coronary artery disease; RCT: randomized controlled trial

The AI tools driving these advances span a hierarchy of techniques. Machine learning (ML) algorithms recognize patterns in structured and unstructured datasets to generate predictions. Deep learning (DL), a subset of ML, employs multilayered neural networks to extract features from complex data such as medical images. Natural language processing and large language models (LLMs) enable interpretation of clinical text, including the extensive clinical data stored in electronic health records (EHRs).[6]

AI-ECG FOR EARLY DETECTION AND SCREENING

The 12-lead electrocardiogram (ECG) is widely available, yet conventional ECG interpretation lacks the sensitivity to detect stable CAD.[7,8] However, DL models can now extract subclinical signatures of coronary atherosclerosis from ECG waveforms that are invisible to expert readers, potentially transforming a routine test into a screening tool for occult disease.[7,8]

Several models have demonstrated this capability. For example, a Taiwanese model detected ≥ 50% coronary artery stenosis by angiography with an area under the receiver operating characteristic curve (AUC/AUROC) of 0.70, improving to 0.72 when combined with cardiovascular risk factors.[7] An Indian ensemble of three AI-ECG models—detecting elevated coronary artery calcium (CAC, AUROC 0.88), obstructive CAD (AUROC 0.85), and regional wall motion abnormalities (AUROC 0.94; internally validated)—provided additive risk stratification beyond the pooled cohort equations. For example, the hazard ratio for acute coronary events was 11.75 in individuals testing positive on all three models.[8] The ECG2CAD model, externally validated in the UK Biobank, achieved AUROCs of 0.747 to 0.782 across three test sets, with the high-risk group showing a 5.59-fold increased risk for myocardial infarction (MI) compared to the low-risk group.[9] Notably, saliency analyses identified QRS amplitudes and P-wave morphology as key discriminators of occult CAD.[9] Most recently, Leasure et al. reported an AI-ECG model achieving an AUC of 0.914 in internal validation for predicting clinically significant CAD (≥ 70% stenosis or ≥ 50% left main stenosis) from a standard 12-lead ECG, although the specific ECG features driving model predictions were not reported.[10] Furthermore, integrated AI-ECG models can predict progression from stable CAD to acute coronary syndrome (AUC 0.953), identifying high-risk outpatients.[11,12] Collectively, these studies suggest that AI-ECG could serve as a low-cost, scalable adjunct for CAD detection and risk prediction. However, the pooled AI-ECG evidence mixes heterogeneous reference standards, and nearly all models derive from referred or angiographically enriched cohorts, introducing spectrum and referral bias. At population-level CAD prevalence, positive predictive value would fall substantially. Prospective validation in unselected populations with calibration and net-benefit assessment is needed before screening deployment.

ELECTRONIC HEALTH RECORDS (EHRs)-BASED DIGITAL MARKERS

Beyond waveform data, ML applied to structured EHR data can generate continuous digital biomarkers of CAD risk. Forrest et al. developed ISCAD (in-silico CAD), an ML-derived continuous marker generated from EHR data that predicted CAD with an AUROC of 0.95 in internal and 0.91 in external validation (UK Biobank).[13] A predecessor model improved 1-year CAD prediction by 12% over the pooled cohort equations and reclassified 25.8% of individuals, with the greatest gains among those classified as low risk.[14] More broadly, ML approaches applied to EHR data have consistently outperformed traditional risk calculators, although challenges in data standardization and prospective validation persist.[6]

AI IN NONINVASIVE CARDIAC IMAGING

Noninvasive cardiac imaging has been the primary gateway to CAD diagnosis, and AI is enhancing every major modality, from automated calcium quantification and computed tomography (CT)-derived physiology to atherosclerotic plaque characterization, echocardiography, and myocardial perfusion scans as well as applications within cardiac magnetic resonance (CMR) imaging.

AUTOMATED CORONARY ARTERY CALCIUM SCORING

Coronary artery calcium (CAC) scoring using the Agatston method is a cornerstone of cardiovascular risk stratification, yet dedicated gated CAC-CT remains underutilized.[15] DL has automated this process: fully automated models applied to ECG-gated CT scans now achieve near-perfect agreement with manual expert scoring, reducing analysis time to seconds.[16] For instance, a DL model demonstrated a pixel-wise, vessel-specific coronary and aortic calcium detection, achieving a Dice score of 0.952 with segmentation in ~4 seconds per individual.[17] More recently, the Agatston 2.0 framework incorporates AI-derived plaque density, morphology, and distribution into a refined calcium score, improving risk discrimination.[15] AI also enables opportunistic CAC detection from the roughly 19 million non-gated chest CTs performed annually in the US for noncardiac indications, with DL-derived CAC ≥ 100 independently associated with increased risk of death,

MI, and stroke.[18] As a result, the 2025 American Heart Association (AHA) scientific statement formally endorsed opportunistic CAC detection and called for systematic reporting and action pathways.[15]

CT-DERIVED FUNCTIONAL AND ANATOMICAL ASSESSMENT

Beyond CAC scoring, AI has expanded the clinical utility of cardiac CT across structural, anatomical, and physiological domains. DL models now segment all four cardiac chambers and left ventricular myocardium from coronary CT angiography (CCTA) with high accuracy, completing analysis in seconds.[19] For coronary artery segmentation and stenosis grading, a DL system quantifies total plaque volume and percent diameter stenosis with excellent agreement with expert readers while reducing analysis time from over 25 minutes to under 6 seconds.[20]

AI-derived CT-based fractional flow reserve (CT-FFR) adds physiological parameters to the detailed anatomy that is provided on CCTA, obtained from already acquired images without additional radiation or contrast exposure to the individual. For instance, a meta-analysis of 43 CT-FFR studies reported overall diagnostic accuracy of 82.2% compared with invasive FFR.[21] DL-based on-site algorithms have further improved performance: Giannopoulos et al. demonstrated an AUC of 0.975 for predicting hemodynamically significant stenosis, with mean CT-FFR analysis time of under 8 minutes per patient.[22] Further, the commercially available DEEPVESSEL-FFR platform (Keya Medical) demonstrated high per-vessel diagnostic accuracy (AUC 0.984), with the combination of CT-FFR and quantitative plaque indices yielding an AUC of 0.888 for predicting 2-year major adverse cardiac events (MACE).[23] A separate 2-year follow-up study demonstrated that a DL-based CT-FFR strategy could have avoided 72% of diagnostic invasive angiograms with comparable MACE rates.[24]

AI IN CT-BASED ATHEROSCLEROTIC PLAQUE CHARACTERIZATION

AI-guided quantitative coronary CT angiography (AI-QCT) enables volumetric, compositional plaque analysis, moving beyond the binary "obstructive vs nonobstructive" paradigm to characterize vulnerable plaque features that drive acute events. AI-QCT plaque staging has predicted 10-year MACE with an AUC of 0.82, significantly outperforming clinical risk factors plus CAC (AUC 0.73, $P < .001$), with patients in the highest plaque stage (percent atheroma volume [PAV] > 15%) carrying a 3.57-fold adjusted hazard for MACE.[25] The CONFIRM2 registry confirmed incremental prognostic value of AI-QCT over CAD-RADS (Coronary Artery Disease–Reporting and Data System) (NRI 0.47), CACS (NRI 0.61), and the modified Duke Index (NRI 0.52) for 3-year MACE.[26] For context, a categorical NRI of 0.47 reflects the net proportion of correctly reclassified participants (summed across events and nonevents) relative to CAD-RADS and should not be interpreted as a 47% gain in overall accuracy; NRI is also sensitive to the choice of risk cut-points. Furthermore, quantitative plaque features extracted from CCTA and incorporated into ML-based prediction models have been found to improve prognostication. In the CREATION registry of 8,431 patients, an XGBoost model incorporating 48 CCTA parameters achieved an AUC of 0.899 for MACE prediction, with lipid plaque burden as the strongest predictor.[27] As such, the 2025 ACC Scientific Statement on Quantitative Coronary Plaque Analysis endorsed AI-assisted plaque quantification for clinical use.[28]

PERICORONARY FAT ATTENUATION INDEX

Coronary inflammation drives plaque vulnerability yet historically is invisible on standard imaging. The pericoronary fat attenuation index (FAI) measures CT attenuation gradients within pericoronary adipose tissue; inflamed coronary arteries shift surrounding fat composition from lipid-dominant to aqueous, increasing CT attenuation in a quantifiable manner.[29] AI has made FAI clinically practical through automated measurement and integration into composite risk scores such as the AI-Risk algorithm (CaRi-Heart, Caristo Diagnostics; CE-marked and deployed in UK NHS hospitals; not cleared by the US Food and Drug Administration [FDA] as of June 2026).[29] The ORFAN study (40,091 patients, median follow-up 2.7 years) externally validated AI-Risk and demonstrated that elevated FAI across all three coronary arteries carried a hazard ratio (HR) of 29.8 for cardiac mortality and 12.6 for MACE.[30] This represents an extreme-group comparison (highest vs lowest FAI quartile across all three vessels) with few events in the reference group; absolute event rates by FAI subgroup were not separately reported. Given the observational design and wide CI, residual confounding cannot be excluded, and prospective interventional testing is needed. These findings were corroborated by a meta-analysis of 15 studies (Table 1).[31]

AI ACROSS OTHER IMAGING MODALITIES

While CT-based applications have seen the most rapid AI development, parallel advances extend across the imaging spectrum. PanEcho, a multitask DL system, performed 18 diagnostic tasks with a median AUC of 0.91 and estimated left ventricular ejection fraction (LVEF) with a mean absolute error of 4.2% while also impressively maintaining performance on point-of-care ultrasound imaging (median AUC 0.85).[32] A blinded randomized trial demonstrated that AI-based LVEF assessment was noninferior to sonographer assessment, with fewer studies requiring substantial

MODALITY	APPLICATION	STUDY/PLATFORM	KEY RESULT	EVIDENCE MATURITY/ STUDY DESIGN
CT-CAC Scoring[16]	Automated CAC from gated and non-gated CT	Kim et al. (2025); n = 1,076 paired scans	Gated: R^2 = 0.995, ICC = 0.997, κ = 0.97, AUROC = 0.99; non-gated (vs manual LDCT): κ = 0.96, AUROC = 0.98–0.99; non-gated (vs gated reference): κ = 0.71-0.88, AUROC = 0.89-0.99 across datasets	Retrospective, internal + external validation
CT-CAC Scoring[69]	Fully automated CAC scoring model	Ihdayhid et al. (2023); n = 1,849	κ = 0.90, ICC = 0.98; 89% correct risk categorization; analysis time 13.1 s/scan	Retrospective, independent test set
CT-CAC Scoring[70]	CAC scoring from CTA (eliminating separate noncontrast scan)	Mu et al. (2022); n = 240	Weighted κ = 0.94; 93% correct risk categorization vs non-\ contrast reference	Retrospective, single center
CT-CAC Scoring[18]	Opportunistic DL-CAC from non-gated chest CT	Peng et al. (2023); n = 5,678	DL-CAC ≥ 100 vs 0: HR 1.51 (95% CI, 1.28-1.79; *P* < .001) for death; HR 1.69 (95% CI, 1.45-1.98) for death/MI/stroke/revasc; only 26% on statins	Retrospective cohort, prognostic
CT-CAC Scoring[17]	Vessel-specific calcium and aortic calcium detection	Singh et al. (2021); n = multicenter	Dice 0.952; segmentation in ~4 s/patient	Retrospective, multicenter validation
CT-CAC (AI-CAC)[48]	AI-CAC: automated plaque characterization + chamber volumetry	Naghavi et al. (2024); n = 5,830 (MESA)	AUC for composite CVD: AI-CAC vs Agatston at 1 yr = 0.784 vs 0.701; 5 years = 0.771 vs 0.709; 10 years = 0.789 vs 0.712; 15 years = 0.816 vs 0.729 (*P* < .0001 for all)	Prospective cohort (MESA), external validation
CT-CAC (Agatston 2.0)[15]	AI-derived plaque density, morphology, and distribution	Foraker et al. (2025)	Improved risk discrimination over traditional Agatston score	AHA Scientific Statement; supporting evidence from prospective cohorts
CT - Chamber Quantification[19]	DL-based cardiac chamber segmentation from CCTA	Baskaran et al. (2020); n = 166	Median Dice 0.92; r = 0.94-0.98 vs manual annotation; analysis in seconds	Retrospective, single center
CT - Stenosis Grading[20]	DL coronary segmentation and stenosis quantification	Lin et al. (2019); n = multicenter	ICC 0.96 (plaque volume), 0.88 (% diameter stenosis) vs experts; ICC 0.95 vs IVUS; mean analysis 5.65 s vs 25.66 min for experts	Retrospective, multicenter validation
CT - FFR[21]	ML-based CT-FFR vs invasive FFR (meta-analysis)	Faulder et al. (2024); 43 studies, n = 5,236	Sensitivity 80.9%, specificity 83.1%, accuracy 82.2%; on-site tools: 84.1% accuracy	Meta-analysis of 43 studies
CT - FFR[22]	DL on-site CT-FFR vs invasive FFR	Giannopoulos et al. (2023)	AUC 0.975, accuracy 95.9% for hemodynamically significant stenosis; AUC 0.991 in heavily calcified vessels (≥ 400 AU); mean analysis < 8 min/patient	Retrospective, single center
CT - FFR[23]	DEEPVESSEL-FFR (Keya Medical) vs invasive FFR	Liu et al. (2023)	r = 0.728 vs invasive FFR; per-vessel AUC 0.984; CT-FFR + quantitative plaque: AUC 0.888 for 2-year MACE	Retrospective cohort with prospective follow-up
CT - FFR[24]	DL CT-FFR strategy vs ICA-guided care (2-year follow-up)	Liu et al. (2021)	72% of diagnostic ICAs avoidable; MACE 2.9% vs 3.3% (*P* = .838)	Retrospective comparative cohort

(Contd.)

MODALITY	APPLICATION	STUDY/PLATFORM	KEY RESULT	EVIDENCE MATURITY/ STUDY DESIGN
CT - Plaque[25]	AI-QCT plaque staging, 10-year outcomes	Nurmohamed et al. (2024); n = multicenter	AUC 0.82 (95% CI, 0.78-0.87) vs clinical + CACS 0.73 (95% CI, 0.68-0.79; *P* < .001); Stage 3 (PAV > 15%): adjusted HR 3.57 (95% CI, 2.12-6.00; *P* < .001); NRI 0.21 (95% CI, 0.09-0.38) over clinical + CACS	Prospective multicenter registry
CT - Plaque[26]	AI-QCT vs CAD-RADS and CACS	CONFIRM2 Registry (2026); n = 1,916	NRI 0.47 over CAD-RADS, 0.61 over CACS, 0.52 over modified Duke Index for 3-year MACE (*P* < .001)	Retrospective multicenter registry
CT - Plaque[27]	XGBoost model with 48 CCTA parameters	CREATION Registry (2025); n = 8,431	AUC 0.899 for MACE prediction; lipid plaque burden strongest predictor (adjusted HR 2.524 per 5% increase; *P* < .001); median follow-up duration: 3.68 years	Retrospective multicenter registry
CT - FAI[30]	Pericoronary FAI + AI-Risk algorithm	ORFAN Study (2024); n = 40,091; median 2.7-year follow-up	3-vessel high FAI: HR 29.8 (95% CI, 13.9-63.9; *P* < .001) for cardiac mortality; HR 12.6 (95% CI, 8.5-18.6; *P* < .001) for MACE	Prospective multicenter cohort
CT - FAI[31]	FAI meta-analysis	Long et al. (2026); 15 studies	Pooled HR 3.28 (95% CI, 2.16-4.97) for MACE	Meta-analysis of 15 studies

Table 1 Summary of key AI applications in CT-based cardiac imaging for coronary artery disease. AI: artificial intelligence; AI-CAC: AI-applied coronary artery calcium; AI-QCT: AI-quantitative computed tomography; AU: Agatston units; AUC: area under the curve; CAC: coronary artery calcium; CACS: coronary artery calcium score; CAD-RADS: Coronary Artery Disease–Reporting and Data System; CCTA: coronary computed tomography angiography; CI: confidence interval; CT: computed tomography; CTA: computed tomography angiography; CVD: cardiovascular disease; DL: deep learning; FAI: fat attenuation index; FFR: fractional flow reserve; HR: hazard ratio; ICA: invasive coronary angiography; ICC: intraclass correlation coefficient; IVUS: intravascular ultrasound; LDCT: low-dose chest CT; MACE: major adverse cardiovascular events; MESA: Multi-Ethnic Study of Atherosclerosis; ML: machine learning; NRI: net reclassification improvement; PAV: percent atheroma volume. Note: Evidence maturity classifications reflect the highest level of evidence for the primary finding reported.

revision (16.8% vs 27.2%, *P* < .001).[33] In single-photon emission computed tomography myocardial perfusion imaging, AI-enhanced perfusion scoring improved AUC for obstructive CAD detection from 0.737 (traditional total perfusion deficit [TPD]) to 0.837 (DL-enhanced TPD).[34] For CMR imaging, automated LVEF showed excellent correlation with CMR reference (R = 0.89) and superior reproducibility compared to manual methods.[35] Table 2 summarizes key AI applications across noninvasive imaging modalities.

AI IN INVASIVE ASSESSMENT AND PROCEDURAL GUIDANCE

The CCL is increasingly augmented by AI tools that support physiological assessment, procedural planning, and real-time guidance, reducing reliance on additional hardware while improving decision-making precision.

WIRE-FREE ANGIOGRAPHY-DERIVED FFR

Invasive FFR is the gold standard for assessing the hemodynamic significance of coronary stenoses but requires adenosine-induced hyperemia and a pressure wire, limiting adoption. Nonhyperemic pressure ratios, such as instantaneous wave-free ratio, eliminated the need for hyperemia but still require a physical wire.[36] AI-powered angiography-derived FFR now enables wire-free physiological assessment directly from diagnostic angiographic images using DL-based 3D coronary reconstruction and computational fluid dynamics. A systematic review demonstrated a pooled AUC of 0.95 against invasive wire-based FFR, significantly outperforming nonhyperemic pressure ratios (AUC 0.85).[36] The landmark ALL-RISE trial, the first prospective randomized trial, randomized 1,930 patients with intermediate stenoses to FFR angio-guided versus pressure wire-guided percutaneous coronary intervention (PCI). The primary composite of all-cause death, MI, or unplanned revascularization occurred in 6.9% versus 7.1% at 1 year (HR 0.98; 95% CI, 0.70-1.39; *P* < .001 for noninferiority; prespecified margin 3.5 percentage points).[37] This trial established wire-free physiological assessment as noninferior to invasive FFR and a clinically validated alternative to broaden adoption of physiology-guided revascularization.

MODALITY	APPLICATION	STUDY/PLATFORM	KEY RESULT	EVIDENCE MATURITY/ STUDY DESIGN
Echo-LVEF[32]	Multitask DL across 18 tasks	PanEcho (2025); 1.2M training videos; tested on 18 tasks	Median AUC 0.91 across 18 tasks; LVEF MAE 4.2%; POCUS median AUC 0.85; outperformed single-task models on 10 of 18 tasks	Retrospective, multi-dataset external validation
Echo-LVEF[33]	AI vs sonographer LVEF (RCT)	He et al. (2023); n = 3,495 studies	AI noninferior to sonographer; fewer studies requiring substantial revision (16.8% vs 27.2%; $P < .001$); mean absolute LVEF difference 1.5%	Blinded RCT
Echo-LVEF + structure[71]	DL prediction of cardiac structure, function, and CV outcomes	Lau et al. (2023); n = 40,000+	Accurate prediction of LV mass, volumes, EF from single-view echo; predicted incident HF (AUC 0.83), AF (AUC 0.77), and death	Retrospective cohort, external validation
Echo-CAD detection[72]	AI stress echo for severe CAD detection	Upton et al. (2022); multicenter	Specificity 92.7%, sensitivity 84.4% for severe CAD; AI assistance increased reader AUC from 0.90 to 0.93	Retrospective, multicenter
Echo-CAD detection[73]	ML-enhanced echo (myocardial work + LA strain)	Guo et al. (2023); n = 818 + 115 validation	AUC 0.852 (test), 0.834 (external validation); sensitivity 0.952; specificity 0.667	Retrospective, external validation
Echo-wall motion[74]	DL for regional wall motion abnormality detection	Kusunose et al. (2020)	Accuracy equal to expert consensus; superior to inexperienced readers; AUC 0.99 (apical 4-chamber), 0.97 (apical 2-chamber)	Retrospective, single center
Nuclear (SPECT)[34]	AI-enhanced perfusion scoring	Miller et al. (2025); n = 555	AUC 0.837 (TPD-DL) vs 0.737 (traditional TPD); $P < .001$; improved per-vessel detection	Retrospective, external validation
Nuclear (SPECT)[75]	DL CAD diagnosis from SPECT-MPI polar maps	Hajianfar et al. (2025); n = 940	Per-vessel AUC 0.89; per-patient AUC 0.83 vs expert reader reference	Retrospective, multicenter
Nuclear (SPECT)[76]	DL bias mitigation in SPECT-MPI	Miller et al. (2023); n = 511 (external test)	AUC 0.930 with augmentation; improved calibration especially in women and across BMI categories	Retrospective, external test set
CMR-LVEF[35]	Automated LVEF vs CMR reference	Sveric et al. (2024)	R = 0.89 with CMR reference; superior reproducibility vs manual methods; mean LVEF difference 0.4%	Retrospective, single center
CMR-segmentation[77]	AI biventricular volumetric analysis (commercial)	Hatipoglu et al. (2022); n = 300	Clinically valid automated segmentation; 250 min (manual) vs 5.8 min (AI) for 20 studies (97.7% time reduction)	Retrospective, single center
CMR-segmentation[78]	DL 3D whole-heart anatomy from CMR	Muffoletto et al. (2024); n = 10,456 (UK Biobank)	Stronger associations with CVD risk factors and disease than standard volumetric measures ($P < .001$)	Retrospective, population cohort
CMR-CAD detection[79]	DL for coronary stenosis detection on coronary MRA	Takafuji et al. (2025); n = 75 (951 segments)	AUC 0.890 for significant stenosis; trainee AUC improved from 0.821 to 0.898 with AI assistance	Retrospective, single center

Table 2 Summary of key AI applications in non-computed tomography cardiac imaging for coronary artery disease. AF: atrial fibrillation; AI: artificial intelligence; AUC: area under the curve; BMI: body mass index; CAD: coronary artery disease; CMR: cardiac magnetic resonance; CV: cardiovascular; CVD: cardiovascular disease; DL: deep learning; Echo: echocardiography; EF: ejection fraction; HF: heart failure; LA: left atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; MAE: mean absolute error; ML: machine learning; MPI: myocardial perfusion imaging; MRA: magnetic resonance angiography; POCUS: point-of-care ultrasound; RCT: randomized controlled trial; SPECT: single-photon emission computed tomography; TPD: total perfusion deficit. Note: Evidence maturity classifications reflect the highest level of evidence for the primary finding reported.

REVASCULARIZATION DECISION SUPPORT

Beyond physiological assessment, AI is being applied to optimize the broader revascularization strategy and predict procedural outcomes. Al'Aref et al. applied ML algorithms to 479,804 patients in the New York PCI Reporting System and demonstrated that a boosted ensemble model (AdaBoost) predicted in-hospital mortality after PCI with an AUC of 0.927, significantly outperforming logistic regression (AUC 0.908, $P < .01$), with direct implications for pre-procedural informed consent and risk communication.[38] Further, Ninomiya et al. developed externally validated ML models using SYNTAX trial data to predict 5-year mortality and identify patients benefiting from coronary artery bypass surgery versus PCI, outperforming the SYNTAX Score II 2020.[39] Additionally, simulations estimate that AI-guided revascularization decisions could shift up to 72.4% of treatment decisions to a more cost-effective strategy.[40]

INTRAVASCULAR IMAGING SEGMENTATION

Intravascular imaging with optical coherence tomography (OCT) and intravascular ultrasound (IVUS) provides high-resolution assessment of atherosclerotic plaque morphology and vessel dimensions, but manual interpretation is time-consuming and operator dependent. AI automates this through the Abbott Ultreon platform, which uses DL to segment OCT images in real time, thus providing a qualitative and quantitative assessment of plaque phenotype, plaque burden, and vessel anatomy to guide vessel preparation and stent sizing.[4] For IVUS imaging, ML-based segmentation achieved 92.4% expert agreement for appropriate balloon sizing.[41] The FLASH (Fully Automated Quantitative Coronary Angiography Versus Optical Coherence Tomography Guidance for Coronary Stent Implantation) trial demonstrated that AI-based fully automated quantitative coronary angiography-assisted PCI achieved noninferior post-PCI minimal stent area compared to OCT-guided PCI; this suggests that AI-angiography may serve as a practical alternative when intravascular imaging is unavailable.[42]

VIRTUAL PCI PLANNING AND CONTRAST STEWARDSHIP

AI-driven computational tools can now simulate post-intervention hemodynamics before stent deployment, predicting post-PCI FFR within ± 0.02 of measured values and allowing operators to test revascularization strategies virtually before committing to a physical intervention.[43] For contrast stewardship, the DCR4Contrast (Dynamic Coronary Roadmap for Contrast Reduction) trial demonstrated that Dynamic Coronary Roadmap (DCR)–guided PCI significantly reduced contrast volume compared to conventional guidance (64.6 vs 90.8 mL; $P < .001$).[44] Figure 2 illustrates the AI-powered CCL workflow across these four domains.[5]

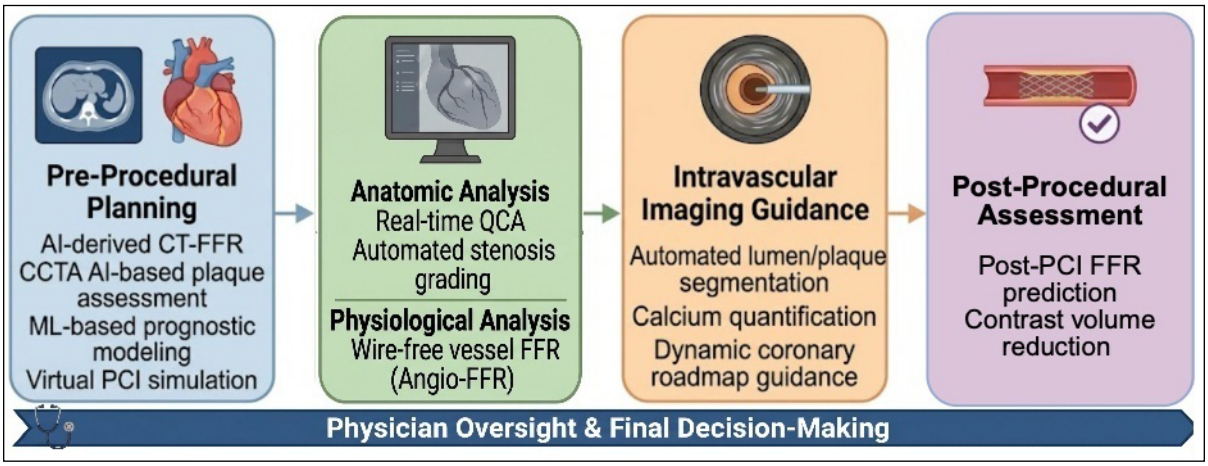


Figure 2 AI-powered catheterization laboratory workflow. A schematic illustration of the four stages of AI integration during percutaneous coronary intervention: pre-procedural planning (including AI-derived CT-FFR, CCTA AI-based plaque assessment, ML-based prognostic modeling, and virtual PCI simulation), anatomic and physiological analysis (real-time QCA, automated stenosis grading, and wire-free vessel FFR via Angio-FFR), intravascular imaging guidance (automated lumen/plaque segmentation, calcium quantification, and dynamic coronary roadmap guidance), and post-procedural assessment (post-PCI FFR prediction and contrast volume reduction). A unifying banner emphasizes physician oversight and final decision-making throughout. Originally created with BioRender.com. Angio-FFR: angiography-derived fractional flow reserve; CCTA: coronary computed tomography angiography; CT-FFR: computed tomography–derived fractional flow reserve; FFR: fractional flow reserve; ML: machine learning; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; QCA: quantitative coronary angiography

AI FOR RISK STRATIFICATION AND PROGNOSTICATION

Accurate risk stratification is essential for guiding the intensity of preventive and therapeutic interventions in CAD. Traditional risk scores rely on limited clinical variables without imaging-derived features, while ML models integrating multimodality imaging data with clinical features have consistently demonstrated superior prognostic performance.[4] To note, high discrimination alone does not establish clinical utility; calibration and decision-curve analyses are needed to confirm benefit at actionable thresholds. Most studies in this space report AUC without calibration or net-benefit data, limiting confidence in clinical readiness. Prospective testing is required.

MACHINE LEARNING INTEGRATING CT AND STRESS MRI DATA

The rapid adoption of CCTA in clinical practice now allows noninvasive evaluation of coronary anatomy and has enabled the development of risk scores that use the presence, extent, and severity of CAD to estimate an individual's risk of incident MACE. In a landmark CONFIRM registry (Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter registry) analysis, Al'Aref et al. demonstrated that an ML model (XGBoost) combining 25 clinical features with CAC scoring predicted obstructive CAD on CCTA with an AUC of 0.881, significantly outperforming the updated Diamond-Forrester model (AUC 0.682) and the CAD Consortium clinical score (AUC 0.734).[45] Furthermore, ML applied to CCTA plaque characteristics demonstrated superior performance compared with conventional CCTA-derived risk scores in predicting death and MI.[4]

ML applied to stress CMR parameters has also shown significant prognostic value. Pezel et al. demonstrated that an ML-derived stress CMR risk score outperformed the Framingham Risk Score for 10-year all-cause mortality, likely because the ML captures myocardial tissue characteristics (scar burden, inducible ischemia, and ventricular volumes) that reflect disease severity beyond what traditional risk factors can estimate.[46] The same group subsequently demonstrated that an ML model integrating both CCTA and stress CMR data achieved a higher AUC (0.86) for 7-year MACE prediction compared with CCTA alone (0.76) or stress CMR alone (0.83), significantly outperforming the Framingham Risk Score, QRISK3, and the European Society of Cardiology score.[47] This multimodal integrated approach may enhance clinicians' ability to identify high-risk individuals with greater diagnostic confidence.

MACHINE LEARNING WITH CALCIUM SCORING AND EPICARDIAL FAT

Beyond CCTA-derived plaque features, AI can extract additional prognostic information from standard noncontrast CAC scans. AI-CAC applies automated calcified plaque characterization, including plaque number, location, density, and number of involved vessels, along with AI-enabled cardiac chamber volumetry to standard CAC scans. AI-CAC was significantly superior to the traditional Agatston score in predicting composite CVD events at 1- through 15-year follow-up.[48]

Epicardial adipose tissue (EAT) is a metabolically active visceral fat depot between the myocardium and the visceral pericardium. Under pathological conditions, EAT promotes local coronary atherosclerosis independent of systemic obesity.[49] AI has enabled rapid, automated EAT quantification from noncontrast CT scans, reducing measurement time from approximately 15 minutes to under 2 seconds, making population-scale assessment feasible.[50] DL-derived EAT volumes have been significantly associated with a composite of cardiac death, MI, and late revascularization (HR 1.35; P = .009), providing complementary and incremental prognostic data to the traditionally used CAC score and atherosclerotic cardiovascular disease risk score.[51]

Moreover, ML integration of CAC and EAT metrics achieved a significantly higher AUC for predicting future MI and/or cardiac death compared with either CAC score or atherosclerotic cardiovascular disease risk score alone.[52] Collectively, these advances highlight the ability of ML to rapidly and accurately synthesize and assimilate prognostic data from routinely acquired images.

AI IN PRECISION THERAPEUTICS AND SECONDARY PREVENTION

AI-DRIVEN PHARMACOGENOMICS FOR PERSONALIZED ANTIPLATELET THERAPY

CYP2C19 loss-of-function (LOF) alleles impair clopidogrel bioactivation, and a meta-analysis of seven randomized controlled trials (~16,000 patients) demonstrated a 30% reduction in ischemic events among LOF carriers treated with ticagrelor or prasugrel versus clopidogrel, with no difference in noncarriers.[53] The prespecified cumulative-events analysis of TAILOR-PCI similarly demonstrated a 39% reduction in cumulative ischemic events in LOF carriers with genotype-guided therapy, without increased bleeding.[54] Reflecting this evidence, the 2024 AHA Scientific Statement now supports CYP2C19 testing to guide P2Y12

inhibitor selection after PCI.[53] AI and ML are expanding this paradigm beyond single-gene testing, enabling polygenic risk scores and ensemble algorithms that integrate multiple pharmacogenes to simultaneously optimize antiplatelet, statin, and anticoagulant dosing therapy—capturing multi-gene influences on drug response that single-gene approaches miss.[4]

Multiomics Integration and Radiomics

Multiomics, the simultaneous analysis of genomic, proteomic, metabolomic, and other molecular data layers, offers a systems-level view of CVD biology that extends beyond any single biomarker or imaging modality.[4] AI is essential to handle the extreme dimensionality of these datasets. The CardiOmicScore, a multitask DL framework applied to UK Biobank data, demonstrated that proteomic and metabolomic risk scores are strong independent CVD predictors (C-index 0.69-0.82 for proteomic scores) and significantly enhance prediction up to 15 years before disease onset when combined with clinical data.[55]

In parallel, CCTA-based radiomics extracts hundreds of quantitative plaque features, describing texture, shape, and spatial heterogeneity at the voxel level and capturing beyond standard attenuation-based measurements.[56] The SCOT-HEART (Scottish Computed Tomography of the HEART) trial derived "eigen radiomic features"—composite variables summarizing clusters of correlated radiomic measurements into a single latent descriptor of plaque phenotype. Eight such features remained independently associated with fatal or nonfatal MI after adjustment for cardiovascular risk score and plaque burden, improving the C-statistic from 0.70 (clinical + plaque burden) to 0.74.[56]

DIGITAL CARDIAC REHABILITATION

AI-powered wearable cardiac rehabilitation addresses the persistent underutilization of traditional center-based programs, with the AHA endorsing remote delivery as showing comparable efficacy to center-based programs.[57] Two recent randomized controlled trials demonstrated that smartwatch-facilitated and wearable-based remote cardiac rehabilitation significantly improved exercise adherence, peak VO_2, and psychological outcomes compared to standard rehabilitation (Table 3).[58,59]

CHALLENGES AND REGULATION

Despite the promise of AI across the CAD care continuum, several critical barriers must be addressed before widespread clinical deployment.

REGULATORY GAPS AND EVIDENTIARY STANDARDS

The regulatory evidence base for cardiovascular AI remains remarkably thin. While 27.3% of FDA-approved AI/ML devices target cardiology, 97.1% received market authorization via the 510(k) pathway, which typically does not require clinical data, and only 3.2% were supported by high-quality clinical trials (Table 4).[60] Furthermore, 95.5% of these lacked demographic transparency.[61] Thus, most clinical AI tools lack prospective clinical testing. The FDA has committed to advancing a tailored regulatory framework for AI-enabled software as a medical device, but regulations trail technology, and existing laws do not yet cover generative AI or its tendency to hallucinate.[4]

IMPLEMENTATION AND HEALTH-ECONOMIC CONSIDERATIONS

Clinical deployment of AI tools faces practical barriers beyond algorithmic performance. Reimbursement pathways remain undefined for most AI-derived outputs (eg, AI-QCT plaque reports, AI-ECG screening scores), limiting adoption incentives. Workflow integration risks alert fatigue when AI outputs are layered onto existing clinical decision points without thoughtful interface design. Infrastructure requirements, including cloud computing and EHR integration, vary widely across health systems and disproportionately disadvantage resource-limited settings.[62] Formal cost-effectiveness analyses remain scarce. While simulation studies suggest AI-guided revascularization decisions may improve cost-efficiency, prospective health-economic evaluations embedded within clinical trials are needed to justify system-level investment.[40]

ALGORITHMIC BIAS AND HEALTH EQUITY

AI models can exhibit strong overall performance while performing poorly for underrepresented populations. The 2024 AHA Scientific Statement identifies three bias layers: societal (systemic discrimination driving differential data quality), statistical (nonrepresentative training samples), and model (ignoring subgroup errors).[6] A systematic review found that 82% of studies in cardiovascular AI exhibited significant racial/ethnic disparities.[63] Thus, the AHA recommends stratified performance reporting by sex, age, and race/ethnicity; diverse training datasets; and participatory frameworks engaging underrepresented communities.[6]

THE BLACK BOX AND VALIDATION GAP

The "black box" nature of DL models complicates clinical trust and medicolegal accountability. Since many AI models lack clear explanations, clinicians struggle to

DOMAIN	APPLICATION	STUDY/PLATFORM	KEY RESULT	EVIDENCE MATURITY/STUDY DESIGN
Pharmacogenomics[53]	CYP2C19-guided P2Y12 inhibitor selection	Meta-analysis of 7 RCTs; n ≈ 16,000	30% reduction in ischemic events in LOF carriers with ticagrelor/prasugrel vs clopidogrel (HR 0.70; 95% CI, 0.59-0.83; *P* interaction < .001); no difference in noncarriers	Meta-analysis of 7 RCTs
Pharmacogenomics[54]	Genotype-guided therapy in LOF carriers	TAILOR-PCI cumulative analysis (2023); n = 5,302	Cumulative ischemic events: HR 0.61 (95% CI, 0.41-0.89; *P* = .011); no excess bleeding (HR 1.36; 95% CI, 0.67-2.76; *P* = .39); 80% reduction in first 3 months (HR 0.21; *P* = .001)	RCT (prespecified cumulative analysis)
Pharmacogenomics[80]	Combined analysis of genotype-guided escalation and de-escalation	Galli et al. TAILOR-PCI + POPular Genetics (2026); n = 6,734; 12-month follow-up	Guided therapy reduced MI (HR 0.68; 95% CI, 0.48-0.97) and NACE (HR 0.85; 95% CI, 0.73-1.00); de-escalation reduced bleeding (HR 0.77; 95% CI, 0.62-0.97) and NACE (HR 0.77; 95% CI, 0.62-0.94)	Combined analysis of 2 RCTs
Multiomics[55]	Proteomic + metabolomic CVD prediction	CardiOmicScore, UK Biobank (2026); 2,920 proteins, 168 metabolites	ProScore C-index 0.69-0.82; MetScore C-index 0.64-0.74; combined with clinical data increased C-index by 0.005–0.102; enhanced prediction up to 15 years before disease onset	Retrospective, population cohort (UK Biobank)
Radiomics[56]	CCTA-based radiomic plaque phenotyping	SCOT-HEART Trial (2025); n = 1,750; median 8.6-year follow-up	8 eigen radiomic features independently associated with fatal/nonfatal MI; C-statistic improved from 0.70 (clinical + plaque burden) to 0.74; greatest discriminatory gains after year 5	Post-hoc analysis of RCT cohort
Radiomics[81]	CCTA radiomic signature for vulnerable plaque and MACE prediction	Chen et al. (2023); n = 708; median 3-year follow-up	AUC 0.75-0.81 for vulnerable plaque detection (IVUS reference); high RS (≥ 1.07): HR 2.01 (*P* = .005) for MACE	Retrospective cohort, external validation
Digital rehabilitation[82]	Network meta-analysis of telehealth CR interventions	Li et al. (2024); 46 RCTs	Wearable + smartphone apps most effective for VO_2 peak (SUCRA 86.8%); improved adherence vs center-based CR	Network meta-analysis of 46 RCTs
Digital rehabilitation[58]	Smartwatch-facilitated home-based CR	Zhang et al. RCT (2025); n = 62	Significant improvement in exercise adherence, peak VO_2, anxiety (*P* = .003), and depression scores (*P* < .01) vs control	RCT
Digital rehabilitation[59]	Wearable remote CR ± online coaching	Nishio et al. RCT (2025); n = 50	Significant peak VO_2 improvement in wearable group; online coaching further enhanced high-intensity physical activity (*P* < .05)	RCT

Table 3 Summary of key AI applications in precision therapeutics and secondary prevention for coronary artery disease. AI: artificial intelligence; AUC: area under the curve; CCTA: coronary computed tomography angiography; CI: confidence interval; CR: cardiac rehabilitation; CVD: cardiovascular disease; CYP2C19: cytochrome P450 2C19; HR: hazard ratio; IVUS: intravascular ultrasound; LOF: loss-of-function; MACE: major adverse cardiovascular events; MI: myocardial infarction; NACE: net adverse cardiovascular events; P2Y12: purinergic receptor P2Y12; RCT: randomized controlled trial; RS: radiomic signature; SUCRA: surface under the cumulative ranking curve; VO_2: peak oxygen consumption. Note: Evidence maturity classifications reflect the highest level of evidence for the primary finding reported.

integrate outputs into their reasoning, and patients cannot provide fully informed consent.[62] Additionally, medicolegal liability of AI-assisted decisions remains unclear.[4] Thus, it is essential that clinical algorithms must complement, not replace, clinician judgment.[62] Robust external validation across diverse populations, prospective clinical trials using SPIRIT-AI and CONSORT-AI reporting standards, and continuous post-market monitoring are critical prerequisites before scaling AI across the CAD care continuum.[64,65]

CLINICAL USE CASE	PRODUCT NAME	MANUFACTURER	FUNCTION	REGULATORY PATHWAY	EVIDENCE MATURITY
CCTA plaque quantification (AI-QCT)[25,26,28]	Cleerly Labs	Cleerly, Inc.	AI-based coronary plaque segmentation, volumetric quantification, and compositional characterization from CCTA	510(k)	Multicenter prospective registries
CCTA plaque quantification (AI-QCT)[25,83]	Cleerly Ischemia	Cleerly, Inc.	ML-based vessel-level probability of flow-limiting CAD from CCTA morphological features	510(k)	Multicenter prospective validation
CCTA plaque quantification[28]	cvi42 Coronary Plaque	Circle Cardiovascular Imaging	Semiautomated coronary plaque segmentation and volumetric analysis from CCTA	510(k)	Retrospective validation
CCTA plaque quantification[28]	Salix	Salix Medical	AI-assisted coronary plaque quantification and characterization from CCTA	510(k)	Retrospective validation
CT-derived FFR[21,84]	HeartFlow FFRCT	HeartFlow, Inc.	CFD-based CT-FFR computation from CCTA; off-site supercomputer processing	510(k)	RCT (PRECISE); prospective multicenter
CT-derived FFR[23,85]	DEEPVESSEL FFR	Keya Medical (Shukun Technology)	DL-based on-site CT-FFR computation from CCTA	510(k) (China; CE Mark)	Prospective single center
CAC scoring[60,69]	AI-CAC (various)	Multiple vendors	Automated Agatston calcium scoring from gated and non-gated CT	510(k)	Retrospective to prospective registry
Angiography-derived FFR[37]	FFRangio	CathWorks Ltd	Wire-free FFR estimation from diagnostic coronary angiography using 3D reconstruction and flow modeling	510(k)	RCT (ALL-RISE)
Angiography-derived FFR[86,87]	QFR (Quantitative Flow Ratio)	Medis Medical Imaging	Wire-free FFR estimation from two angiographic projections using computational modeling	510(k) (CE Mark)	RCT (FAVOR III China; FAVOR III Europe)
Angiography-derived FFR[88]	CAAS vFFR	Pie Medical Imaging	Wire-free vessel FFR estimation from two angiographic projections	510(k) (CE Mark)	RCT (FAST III)
Echocardiography[72,89]	EchoGo Core	Ultromics	AI-based automated echocardiographic measurements and stress echo CAD detection	510(k)	Retrospective multicenter; prospective RCT ongoing (PROTEUS)
Echocardiography[33,90]	Caption Guidance/ EchoMD AutoEF	Caption Health (GE HealthCare)	DL-guided echocardiographic image acquisition and automated LVEF measurement	De novo/510(k)	Prospective validation
Pericoronary inflammation[29,30]	CaRi-Heart	Caristo Diagnostics	Standardized FAI mapping and AI-Risk cardiovascular risk prediction from CCTA	CE Mark (not FDA-cleared)	Multicenter prospective cohort (ORFAN)

Table 4 Selected AI/ML devices that have received FDA 510(k) clearance for CAD-related applications. AI: artificial intelligence; AI-CAC: AI-applied coronary artery calcium; AI-QCT: AI-quantitative computed tomography; CAC: coronary artery calcium; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CE: Conformité Européenne; CFD: computational fluid dynamics; CT: computed tomography; DL: deep learning; FAI: fat attenuation index; FFR: fractional flow reserve; LVEF: left ventricular ejection fraction; ML: machine learning. Note: This table is not exhaustive. Regulatory status reflects publicly available information as of June 2026 and may have changed. Some products listed with CE Mark or China clearance may not yet have FDA 510(k) clearance; "510(k)" denotes US FDA clearance specifically. Inclusion does not constitute endorsement.

FUTURE DIRECTIONS

Generative AI and LLMs can reshape clinical documentation and decision support in CAD. AI telescribing may reduce documentation burden, while vision-to-language models can automate echo reporting.[62] ChatGPT-4 achieved 82% agreement with heart teams in one study but only 65% accuracy for multivessel CAD, emphasizing that physician oversight remains essential.[66,67] General-purpose LLMs are not cleared medical devices, are prone to hallucination, and must not inform revascularization decisions outside validated, governed workflows. Effective governance should include scheduled monitoring for model-drift, predefined oversight checkpoints before clinical action, and clear ML-operations accountability chains that assign responsibility for algorithm performance.

Beyond decision support, agentic AI—systems capable of autonomously analyzing data and coordinating clinical workflows—has been emerging, although clinical implementation remains limited.[68] Over-reliance on AI raises concerns for deskilling, never-skilling, and mis-skilling, particularly among trainees.[62] Physician-in-the-loop governance should include prospective drift monitoring with predefined revalidation triggers, mandatory human oversight at key decision nodes, and institutional ML operations accountability for algorithm performance. Moreover, CAD management requires contextual judgment integrating patient autonomy, psychosocial factors, and comorbidity interactions that current AI systems cannot fully capture.

Foundation models trained on multimodal data (ECG, imaging, genomics, EHR) represent the next frontier.[4] Digital twin technologies simulating personalized disease trajectories could accelerate clinical trial design and enable virtual testing of interventions before bedside deployment.[4] AI-optimized trials leveraging automated eligibility screening and LLM-based event adjudication may accelerate the drug development timeline.[4] Furthermore, the growing computational demands of complex AI models raise environmental sustainability concerns. Realizing this vision will require equity-centered deployment, ensuring that these advances reach diverse and underserved populations (Figure 3).[5]

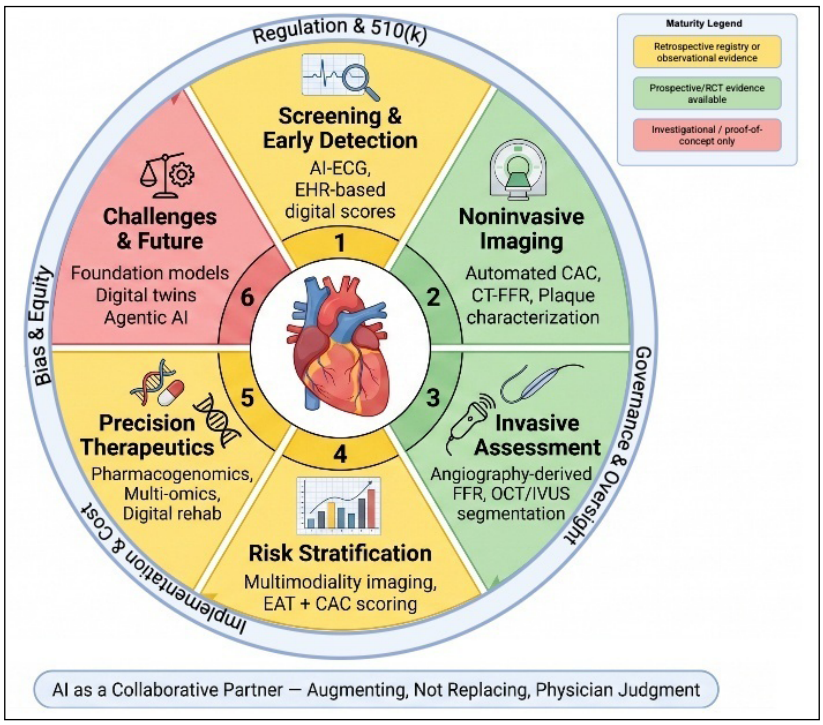


Figure 3 Central illustration: Artificial intelligence across the coronary artery disease care continuum. A six-domain radial framework depicting AI applications organized as numbered sectors: (1) screening and early detection (AI-ECG, EHR-based digital scores), (2) noninvasive imaging (automated CAC, CT-FFR, plaque characterization), (3) invasive assessment (angiography-derived FFR, OCT/IVUS segmentation), (4) risk stratification (multimodality imaging, EAT + CAC scoring), (5) precision therapeutics (pharmacogenomics, multiomics, digital rehabilitation), and (6) challenges and future directions (foundation models, digital twins, agentic AI). An outer ring highlights cross-cutting implementation themes: regulation and 510(k), governance and oversight, implementation and cost, and bias and equity. A color-coded maturity legend indicates evidence levels: yellow (retrospective registry or observational evidence), green (prospective/RCT evidence available), and red (investigational/proof-of-concept only). Originally created with BioRender.com. AI-ECG: artificial intelligence–enhanced electrocardiography; CAC: coronary artery calcium; CT-FFR: computed tomography–derived fractional flow reserve; EAT: epicardial adipose tissue; EHR: electronic health record; IVUS: intravascular ultrasound; ML: machine learning; OCT: optical coherence tomography; RCT: randomized controlled trial

CONCLUSION

AI has demonstrated the capacity to enhance every stage of the CAD care continuum, from early detection via AI-ECG and opportunistic calcium scoring, through noninvasive plaque characterization and functional assessment, to catheterization laboratory guidance and personalized secondary prevention strategies. Importantly, these applications differ markedly in evidentiary maturity: only a subset (opportunistic and automated calcium scoring, AI-based LVEF quantification, CT-derived FFR, and angiography-derived FFR) are supported by prospective or randomized data, whereas foundation models, digital twins, agentic workflows, and multiomics integration remain investigational. The next phase of CAD-AI research must move beyond model discrimination toward prospective evidence that AI changes clinician behavior, improves patient outcomes, reduces unnecessary testing, and performs equitably across populations. Realizing its full potential requires diverse randomized trials with hard end points, transparent subgroup reporting, equity-centered implementation, and governance frameworks—including drift monitoring and defined oversight checkpoints—that maintain the physician as the final decision-maker. The ultimate goal is not to replace clinical judgment but to augment it, transforming AI into a continuous, clinician-in-the-loop partner across the entire trajectory of CAD.

KEY POINTS

- Artificial intelligence (AI)-electrocardiogram and electronic health record-based digital markers enable earlier detection of significant coronary artery disease (CAD) from routine clinical data.
- AI-enhanced noninvasive imaging, including automated calcium scoring, computed tomography-derived fractional flow reserve (FFR), and plaque characterization, improves diagnostic accuracy and functional assessment while reducing invasive procedures.
- Wire-free angiography-derived FFR and AI-guided intravascular imaging segmentation support real-time procedural decisions.
- Machine learning models integrating multimodality imaging and clinical data outperform traditional risk calculators for predicting major adverse cardiac events.
- High discriminative performance (area under the receiver operating characteristic curve) does not equate to clinical readiness; the next phase of CAD-AI research must demonstrate that AI changes clinician behavior, improves outcomes, and performs equitably—with physicians remaining the final decision-makers.

COMPETING INTERESTS

Subhi J. Al'Aref receives royalty fees from Elsevier. The other authors have no competing interests to declare.

AUTHOR AFFILIATIONS

Keshav Garg, MD orcid.org/0000-0003-1995-1626
Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Landon Bruich, MD orcid.org/0009-0009-5743-2019
Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Luke J. Enemark, BA orcid.org/0009-0008-3358-0300
School of Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Khalid Sawalha, MD orcid.org/0000-0002-1234-9133
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Aakash Rana, MD orcid.org/0009-0001-4167-1164
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Ankit Agrawal, MD orcid.org/0000-0001-7885-6667
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Robert F. Spraggins II, MD orcid.org/0009-0001-0864-2476
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Osama Khalaila, MD orcid.org/0000-0003-1987-8625
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Mohanad Shehadeh, MD orcid.org/0009-0005-0861-9072
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Buthainah Alhwarat, MD orcid.org/0009-0002-4264-2063
Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Carsten Johnson, BS orcid.org/0009-0002-8367-095X
School of Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Avirup Guha, MD, MPH orcid.org/0000-0003-0253-1174
Division of Cardiology, Department of Medicine, Medical College of Georgia at Augusta University, Augusta, Georgia, US

Yiye Zhang, MS, PhD orcid.org/0000-0003-3494-2699
Division of Health Informatics, Department of Population Health Sciences, Weill Cornell Medicine, New York, New York, US

Gianluca Pontone, MD, PhD orcid.org/0000-0002-1339-6679
Department of Perioperative Cardiology and Cardiovascular Imaging, Centro Cardiologico Monzino IRCCS, Italy; Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

Sourbha S. Dani, MD, MSc orcid.org/0000-0002-3434-6136
Division of Cardiology, Lahey Hospital & Medical Center, Beth Israel Lahey Health, Burlington, Massachusetts, US

Vignesh Chindambaram, MD, MPH orcid.org/0000-0002-4240-1027
Division of Cardiology, Department of Medicine, John H. Stroger Hospital of Cook County, Chicago, Illinois, US

Lohendran Baskaran, MBBS orcid.org/0000-0003-0565-7151
Cardiovascular Systems Imaging and Artificial Intelligence Lab, National Heart Research Institute Singapore, National Heart Centre Singapore; Department of Cardiology, National Heart Centre Singapore; SingHealth Duke-National University of Singapore Cardiovascular Sciences Academic Clinical Programme, Duke-National University of Singapore Medical School, National University of Singapore, Singapore

Bhupendar Tayal, MD, PhD orcid.org/0000-0002-6594-6177
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

Subhi J. Al'Aref, MD orcid.org/0009-0003-6667-2037
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, US

REFERENCES

1. **Martin SS, Aday AW, Almarzooq ZI,** et al. 2024 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. Circulation. 2024 Feb 20;149(8):e347-e913. doi: 10.1161/CIR.0000000000001209
2. **Dagenais GR, Leong DP, Rangarajan S,** et al. Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. Lancet. 2020 Mar 7;395(10226):785-794. doi: 10.1016/S0140-6736(19)32007-0
3. **Dimala CA, Reggio C, Changoh M, Donato A.** Trends and Disparities in CAD and AMI in the United States From 2000 to 2020. JACC Adv. 2024 Dec;3(12):101373. doi: 10.1016/j.jacadv.2024.101373
4. **Khera R, Oikonomou EK, Nadkarni GN,** et al. Transforming Cardiovascular Care With Artificial Intelligence: From Discovery to Practice: JACC State-of-the-Art Review. J Am Coll Cardiol. 2024 Jul 2;84(1):97-114. doi: 10.1016/j.jacc.2024.05.003
5. **BioRender.com** [Internet]. Toronto, ON: Biorender Science Suite, Inc.; c2026. cited 2026 Jun 15. Available from: https://www.biorender.com/
6. **Armoundas AA, Narayan SM, Arnett DK,** et al. Use of Artificial Intelligence in Improving Outcomes in Heart Disease: A Scientific Statement From the American Heart Association. Circulation. 2024 Apr 2;149(14):e1028-e1050. doi: 10.1161/CIR.0000000000001201
7. **Lee YH, Hsieh MT, Chang CC,** et al. Improving detection of obstructive coronary artery disease with an artificial intelligence-enabled electrocardiogram algorithm. Atherosclerosis. 2023 Sep;381:117238. doi: 10.1016/j.atherosclerosis.2023.117238
8. **Awasthi S, Sachdeva N, Gupta Y,** et al. Identification and risk stratification of coronary disease by artificial intelligence-enabled ECG. EClinicalMedicine. 2023 Oct 24;65:102259. doi: 10.1016/j.eclinm.2023.102259
9. **Kany S, Friedman SF, Al-Alusi M,** et al. Electrocardiogram-Based Artificial Intelligence to Identify Coronary Artery Disease. JACC Adv. 2025 Sep;4(9):102041. doi: 10.1016/j.jacadv.2025.102041
10. **Leasure M, Poornima I, Butchy A,** et al. Use of Electrocardiograms to Identify Coronary Artery Disease: Cross-Validation of an Artificial Intelligence Model. JACC Adv. 2026 Mar;5(3):102573. doi: 10.1016/j.jacadv.2025.102573
11. **Ma H, Bai H, Yan J,** et al. AI approaches for predicting progression to acute coronary syndrome among stable coronary heart disease patients. NPJ Cardiovasc Health. 2025 Dec 2;2:59. doi: 10.1038/s44325-025-00094-2
12. **Garg K, Bhanushali V, Gautam N,** et al. AI-enhanced ECG for acute coronary syndrome triage: A state-of-the-art review. Cardiovasc Revasc Med. 2026 Jun 24:S1553-S8389(26)00281-2. doi: 10.1016/j.carrev.2026.06.015
13. **Forrest IS, Petrazzini BO, Duffy Á,** et al. Machine learning-based marker for coronary artery disease: derivation and validation in two longitudinal cohorts. Lancet. 2023 Jan 21;401(10372):215-225. doi: 10.1016/S0140-6736(22)02079-7
14. **Petrazzini BO, Chaudhary K, Márquez-Luna C,** et al. Coronary Risk Estimation Based on Clinical Data in Electronic Health Records. J Am Coll Cardiol. 2022 Mar 29;79(12):1155-1166. doi: 10.1016/j.jacc.2022.01.021
15. **Foraker R, Sperling L, Bratzke L,** et al. Opportunistic Detection of Coronary Artery Calcium on Noncardiac Chest Computed Tomography: An Emerging Tool for Cardiovascular Disease Prevention: A Scientific Statement From the American Heart Association. Circulation. 2025 Nov 11;152(19):e391-e401. doi: 10.1161/CIR.0000000000001382
16. **Kim S, Park EA, Ahn C,** et al. Performance of fully automated deep-learning-based coronary artery calcium scoring in ECG-gated calcium CT and non-gated low-dose chest CT. Eur Radiol. 2025 Nov;35(11):7084-7095. doi: 10.1007/s00330-025-11559-4
17. **Singh G, Al'Aref SJ, Lee BC,** et al. End-to-End, Pixel-Wise Vessel-Specific Coronary and Aortic Calcium Detection and Scoring Using Deep Learning. Diagnostics. 2021 Feb 2;11(2):215. doi: 10.3390/diagnostics11020215
18. **Peng AW, Dudum R, Jain SS,** et al. Association of Coronary Artery Calcium Detected by Routine Ungated CT Imaging With Cardiovascular Outcomes. J Am Coll Cardiol. 2023 Sep 19;82(12):1192-11202. doi: 10.1016/j.jacc.2023.06.040
19. **Baskaran L, Maliakal G, Al'Aref SJ,** et al. Identification and Quantification of Cardiovascular Structures From CCTA: An End-to-End, Rapid, Pixel-Wise, Deep-Learning Method. JACC Cardiovasc Imaging. 2020 May;13(5):1163-1171. doi: 10.1016/j.jcmg.2019.08.025
20. **Lin A, Manral N, McElhinney P,** et al. Deep learning-enabled coronary CT angiography for plaque and stenosis quantification and cardiac risk prediction: an international multicentre study. Lancet Digit Health. 2022 Apr;4(4):e256-e265. doi: 10.1016/S2589-7500(22)00022-X

21. **Faulder TI, Prematunga K, Moloi SB, Faulder LE, Jones R, Moxon JV.** Agreement of Fractional Flow Reserve Estimated by Computed Tomography With Invasively Measured Fractional Flow Reserve: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2024 May 21;13(10):e034552. doi: 10.1161/JAHA.124.034552
22. **Giannopoulos AA, Keller L, Sepulcri D,** et al. High-Speed On-Site Deep Learning-Based FFR-CT Algorithm: Evaluation Using Invasive Angiography as the Reference Standard. AJR Am J Roentgenol. 2023 Oct;221(4):460-470. doi: 10.2214/AJR.23.29156
23. **Liu M, Li R, Bai C,** et al. Predictive value of DEEPVESSEL-fractional flow reserve and quantitative plaque analysis based on coronary CT angiography for major adverse cardiac events. Clin Radiol. 2023 Sep;78(9):e600-e607. doi: 10.1016/j.crad.2023.04.013
24. **Liu X, Mo X, Zhang H, Yang G, Shi C, Hau WK.** 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 Sep;31(9):7039-7046. doi: 10.1007/s00330-021-07771-7
25. **Nurmohamed NS, Bom MJ, Jukema RA,** et al. AI-Guided Quantitative Plaque Staging Predicts Long-Term Cardiovascular Outcomes in Patients at Risk for Atherosclerotic CVD. JACC Cardiovasc Imaging. 2024 Mar;17(3):269-280. doi: 10.1016/j.jcmg.2023.05.020
26. **van Rosendael A, Nakanishi R, Bax JJ,** et al. Prognostic Value of AI-Based Quantitative Coronary CTA vs Human Reader-Based Visual Assessment: Results From the CONFIRM2 Registry. JACC Cardiovasc Imaging. 2026 Mar;19(3):345-359. doi: 10.1016/j.jcmg.2025.09.021
27. **Song Y, Xu N, Zheng J,** et al. Machine Learning Model for Atherosclerosis Evaluation and Cardiovascular Risk Prediction Based on Coronary CT Angiography-Analysis From the CREATION Registry. Circ Cardiovasc Imaging. 2025 Dec;18(12):e018443. doi: 10.1161/CIRCIMAGING.125.018443
28. **Chandrashekhar Y, Blankstein R, Shaw LJ,** et al. Quantitative Coronary Plaque Analysis in Clinical Practice: 2025 ACC Scientific Statement. JACC Cardiovasc Imaging. 2026 May;19(5):637-652. doi: 10.1016/j.jcmg.2025.11.008
29. **Oikonomou EK, Antonopoulos AS, Schottlander D,** et al. Standardized measurement of coronary inflammation using cardiovascular computed tomography: integration in clinical care as a prognostic medical device. Cardiovasc Res. 2021 Nov 22;117(13):2677-2690. doi: 10.1093/cvr/cvab286
30. **Chan K, Wahome E, Tsiachristas A,** et al. Inflammatory risk and cardiovascular events in patients without obstructive coronary artery disease: the ORFAN multicentre, longitudinal cohort study. Lancet. 2024 Jun 15;403(10444):2606-2618. doi: 10.1016/S0140-6736(24)00596-8
31. **Long Q, Yu M, Xiong YY,** et al. Pericoronary fat attenuation index is a potential indicator for the prognosis of coronary heart disease: a systematic review and meta-analysis. Clin Radiol. 2026 Jun;97:107310. doi: 10.1016/j.crad.2026.107310
32. **Holste G, Oikonomou EK, Tokodi M, Kovács A, Wang Z, Khera R.** Complete AI-Enabled Echocardiography Interpretation With Multitask Deep Learning. JAMA. 2025 Jul 22;334(4):306-318. doi: 10.1001/jama.2025.8731
33. **He B, Kwan AC, Cho JH,** et al. Blinded, randomized trial of sonographer versus AI cardiac function assessment. Nature. 2023 Apr;616(7957):520-524. doi: 10.1038/s41586-023-05947-3
34. **Miller RJH, Kavanagh P, Lemley M,** et al. Artificial Intelligence-Enhanced Perfusion Scoring Improves the Diagnostic Accuracy of Myocardial Perfusion Imaging. J Nucl Med Off Publ Soc Nucl Med. 2025 Apr 1;66(4):648-653. doi: 10.2967/jnumed.124.268079
35. **Sveric KM, Ulbrich S, Dindane Z,** et al. Improved assessment of left ventricular ejection fraction using artificial intelligence in echocardiography: A comparative analysis with cardiac magnetic resonance imaging. Int J Cardiol. 2024 Jan 1;394:131383. doi: 10.1016/j.ijcard.2023.131383
36. **Li W, Takahashi T, Sehatbakhsh S,** et al. Diagnostic performances of Nonhyperemic Pressure Ratios and Coronary Angiography-Based Fractional Flow Reserve against conventional Wire-Based Fractional Flow Reserve. Coron Artery Dis. 2024 Mar 1;35(2):83-91. doi: 10.1097/MCA.0000000000001309
37. **Fearon WF, Jeremias A, Witberg G,** et al. Angiography-Derived Fractional Flow Reserve to Guide PCI. N Engl J Med. 2026 Jul 2;395(1):9-19. doi: 10.1056/NEJMoa2600949
38. **Al'Aref SJ, Singh G, van Rosendael AR,** et al. Determinants of In-Hospital Mortality After Percutaneous Coronary Intervention: A Machine Learning Approach. J Am Heart Assoc. 2019 Mar 5;8(5):e011160. doi: 10.1161/JAHA.118.011160
39. **Ninomiya K, Kageyama S, Shiomi H,** et al. Can Machine Learning Aid the Selection of Percutaneous vs Surgical Revascularization? J Am Coll Cardiol. 2023 Nov 28;82(22):2113-2124. doi: 10.1016/j.jacc.2023.09.818
40. **Mullie T, Puri A, Bogner E,** et al. Health economic simulation modeling of an AI-enabled clinical decision support system for coronary revascularization. NPJ Digit Med. 2026 Feb 16;9(1):249. doi: 10.1038/s41746-026-02430-x
41. **Matsumura M, Mintz GS, Dohi T,** et al. Accuracy of IVUS-Based Machine Learning Segmentation Assessment of Coronary Artery Dimensions and Balloon Sizing. JACC Adv. 2023 Sep;2(7):100564. doi: 10.1016/j.jacadv.2023.100564
42. **Kim Y, Yoon HJ, Suh J,** et al. Artificial Intelligence-Based Fully Automated Quantitative Coronary Angiography vs Optical Coherence Tomography-Guided PCI: The FLASH Trial. JACC Cardiovasc Interv. 2025 Jan 27;18(2):187-197. doi: 10.1016/j.jcin.2024.10.025

43. **Gosling RC, Morris PD, Silva Soto DA, Lawford PV, Hose DR, Gunn JP.** Virtual Coronary Intervention: A Treatment Planning Tool Based Upon the Angiogram. JACC Cardiovasc Imaging. 2019 May;12(5):865-872. doi: 10.1016/j.jcmg.2018.01.019
44. **Hennessey B, Danenberg H, De Vroey F,** et al. Dynamic Coronary Roadmap versus standard angiography for percutaneous coronary intervention: the randomised, multicentre DCR4Contrast trial. EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol. 2024 Feb 5;20(3):e198-e206. doi: 10.4244/EIJ-D-23-00460
45. **Al'Aref SJ, Maliakal G, Singh G,** et al. Machine learning of clinical variables and coronary artery calcium scoring for the prediction of obstructive coronary artery disease on coronary computed tomography angiography: analysis from the CONFIRM registry. Eur Heart J. 2020 Jan 14;41(3):359-367. doi: 10.1093/eurheartj/ehz565
46. **Pezel T, Sanguineti F, Garot P,** et al. Machine-Learning Score Using Stress CMR for Death Prediction in Patients With Suspected or Known CAD. JACC Cardiovasc Imaging. 2022 Nov;15(11):1900-1913. doi: 10.1016/j.jcmg.2022.05.007
47. **Pezel T, Toupin S, Bousson V,** et al. A Machine Learning Model Using Cardiac CT and MRI Data Predicts Cardiovascular Events in Obstructive Coronary Artery Disease. Radiology. 2025 Jan;314(1):e233030. doi: 10.1148/radiol.233030
48. **Naghavi M, Reeves AP, Atlas K,** et al. Artificial intelligence applied to coronary artery calcium scans (AI-CAC) significantly improves cardiovascular events prediction. NPJ Digit Med. 2024 Nov 5;7(1):309. doi: 10.1038/s41746-024-01308-0
49. **Iacobellis G.** Epicardial adipose tissue in contemporary cardiology. Nat Rev Cardiol. 2022 Sep;19(9):593-606. doi: 10.1038/s41569-022-00679-9
50. **Miller RJH, Shanbhag A, Killekar A,** et al. AI-derived epicardial fat measurements improve cardiovascular risk prediction from myocardial perfusion imaging. NPJ Digit Med. 2024 Feb 3;7(1):24. doi: 10.1038/s41746-024-01020-z
51. **Eisenberg E, McElhinney PA, Commandeur F,** et al. Deep Learning-Based Quantification of Epicardial Adipose Tissue Volume and Attenuation Predicts Major Adverse Cardiovascular Events in Asymptomatic Subjects. Circ Cardiovasc Imaging. 2020 Feb;13(2):e009829. doi: 10.1161/CIRCIMAGING.119.009829
52. **Commandeur F, Slomka PJ, Goeller M,** et al. Machine learning to predict the long-term risk of myocardial infarction and cardiac death based on clinical risk, coronary calcium, and epicardial adipose tissue: a prospective study. Cardiovasc Res. 2020 Dec 1;116(14):2216-2225. doi: 10.1093/cvr/cvz321
53. **Pereira NL, Cresci S, Angiolillo DJ,** et al. CYP2C19 Genetic Testing for Oral P2Y12 Inhibitor Therapy: A Scientific Statement From the American Heart Association. Circulation. 2024 Aug 6;150(6):e129-e150. doi: 10.1161/CIR.0000000000001257
54. **Ingraham BS, Farkouh ME, Lennon RJ,** et al. Genetic-Guided Oral P2Y12 Inhibitor Selection and Cumulative Ischemic Events After Percutaneous Coronary Intervention. JACC Cardiovasc Interv. 2023 Apr 10;16(7):816-825. doi: 10.1016/j.jcin.2023.01.356
55. **Luo Y, Zhang N, Yang J,** et al. AI-based multiomics profiling reveals complementary omics contributions to personalized prediction of cardiovascular disease. Nat Commun. 2026 Feb 2;17(1):2269. doi: 10.1038/s41467-026-68956-6
56. **Kolossváry M, Lin A, Kwiecinski J,** et al. Coronary Plaque Radiomic Phenotypes Predict Fatal or Nonfatal Myocardial Infarction: Analysis of the SCOT-HEART Trial. JACC Cardiovasc Imaging. 2025 Mar;18(3):308-319. doi: 10.1016/j.jcmg.2024.08.012
57. **Golbus JR, Lopez-Jimenez F, Barac A,** et al. Digital Technologies in Cardiac Rehabilitation: A Science Advisory From the American Heart Association. Circulation. 2023 Jul 4;148(1):95-107. doi: 10.1161/CIR.0000000000001150
58. **Zhang S, Wang Y, Wu J, Ma C, Meng X.** Effectiveness of Smartwatch Device on Adherence to Home-Based Cardiac Rehabilitation in Patients With Coronary Heart Disease: Randomized Controlled Trial. JMIR MHealth UHealth. 2025 Sep 18;13:e70848. doi: 10.2196/70848
59. **Nishio R, Dohi T, Yokoyama M,** et al. Wearable Devices in Remote Cardiac Rehabilitation With and Without Weekly Online Coaching for Patients With Coronary Artery Disease: Randomized Controlled Trial. JMIR MHealth UHealth. 2025 May 12;13:e63797. doi: 10.2196/63797
60. **Hussain A, Guni A, Gandhewar R,** et al. Is the FDA regulation of cardiology AI devices supporting cardiovascular innovation: a scoping review. Heart. 2026 Feb 23;112(6):300-306. doi: 10.1136/heartjnl-2025-326307
61. **Patel NN.** Bias, External Validation, and Real-World Implementation of Artificial Intelligence Models in Cardiovascular Medicine. Am J Cardiol. 2026 Jun 8;S0002-9149(26)00392-9. doi: 10.1016/j.amjcard.2026.06.005
62. **Jain SS, Elias P, Poterucha T,** et al. Artificial Intelligence in Cardiovascular Care-Part 2: Applications: JACC Review Topic of the Week. J Am Coll Cardiol. 2024 Jun 18;83(24):2487-2496. doi: 10.1016/j.jacc.2024.03.401
63. **Cau R, Pisu F, Suri JS, Saba L.** Addressing hidden risks: Systematic review of artificial intelligence biases across racial and ethnic groups in cardiovascular diseases. Eur J Radiol. 2025 Feb;183:111867. doi: 10.1016/j.ejrad.2024.111867
64. **Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK, SPIRIT-AI and CONSORT-AI Working Group.** Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. Nat Med.

2020 Sep;26(9):1364-1374. doi: 10.1038/s41591-020-1034-x

65. **Rivera SC, Liu X, Chan AW, Denniston AK, Calvert MJ, SPIRIT-AI and CONSORT-AI Working Group.** Guidelines for clinical trial protocols for interventions involving artificial intelligence: the SPIRIT-AI Extension. BMJ. 2020 Sep 9;370:m3210. doi: 10.1136/bmj.m3210
66. **Sudri K, Motro-Feingold I, Ramon-Gonen R,** et al. Enhancing Coronary Revascularization Decisions: The Promising Role of Large Language Models as a Decision-Support Tool for Multidisciplinary Heart Team. Circ Cardiovasc Interv. 2024 Nov;17(11):e014201. doi: 10.1161/CIRCINTERVENTIONS.124.014201
67. **Migliaro S, Celotto R, Teliti R, Mariani S, Altamura L, Tomai F.** Comparing AI-Driven and Heart Team Decision-Making in Multivessel Coronary Artery Disease. J Clin Med. 2025 Jun 23;14(13):4452. doi: 10.3390/jcm14134452
68. **Collaco BG, Haider SA, Prabha S,** et al. The role of agentic artificial intelligence in healthcare: a scoping review. NPJ Digit Med. 2026 Mar 14;9(1):345. doi: 10.1038/s41746-026-02517-5
69. **Ihdayhid AR, Lan NSR, Williams M,** et al. Evaluation of an artificial intelligence coronary artery calcium scoring model from computed tomography. Eur Radiol. 2023 Jan;33(1):321-329. doi: 10.1007/s00330-022-09028-3
70. **Mu D, Bai J, Chen W,** et al. Calcium Scoring at Coronary CT Angiography Using Deep Learning. Radiology. 2022 Feb;302(2):309-316. doi: 10.1148/radiol.2021211483
71. **Lau ES, Di Achille P, Kopparapu K,** et al. Deep Learning-Enabled Assessment of Left Heart Structure and Function Predicts Cardiovascular Outcomes. J Am Coll Cardiol. 2023 Nov 14;82(20):1936-1948. doi: 10.1016/j.jacc.2023.09.800
72. **Upton R, Mumith A, Beqiri A,** et al. Automated Echocardiographic Detection of Severe Coronary Artery Disease Using Artificial Intelligence. JACC Cardiovasc Imaging. 2022 May;15(5):715-727. doi: 10.1016/j.jcmg.2021.10.013
73. **Guo Y, Xia C, Zhong Y,** et al. Machine learning-enhanced echocardiography for screening coronary artery disease. Biomed Eng Online. 2023 May 11;22(1):44. doi: 10.1186/s12938-023-01106-x
74. **Kusunose K, Abe T, Haga A,** et al. A Deep Learning Approach for Assessment of Regional Wall Motion Abnormality From Echocardiographic Images. JACC Cardiovasc Imaging. 2020 Feb;13(2 Pt 1):374-381. doi: 10.1016/j.jcmg.2019.02.024
75. **Hajianfar G, Gharibi O, Sabouri M,** et al. Artificial intelligence-powered coronary artery disease diagnosis from SPECT myocardial perfusion imaging: a comprehensive deep learning study. Eur J Nucl Med Mol Imaging. 2025 Jul;52(8):3019-3035. doi: 10.1007/s00259-025-07145-x
76. **Miller RJH, Singh A, Otaki Y,** et al. Mitigating bias in deep learning for diagnosis of coronary artery disease from myocardial perfusion SPECT images. Eur J Nucl Med Mol Imaging. 2023 Jan;50(2):387-397. doi: 10.1007/s00259-022-05972-w
77. **Hatipoglu S, Mohiaddin RH, Gatehouse P,** et al. Performance of artificial intelligence for biventricular cardiovascular magnetic resonance volumetric analysis in the clinical setting. Int J Cardiovasc Imaging. 2022 Nov;38(11):2413-2424. doi: 10.1007/s10554-022-02649-1
78. **Muffoletto M, Xu H, Burns R,** et al. Evaluation of deep learning estimation of whole heart anatomy from automated cardiovascular magnetic resonance short- and long-axis analyses in UK Biobank. Eur Heart J Cardiovasc Imaging. 2024 Sep 30;25(10):1374-1383. doi: 10.1093/ehjci/jeae123
79. **Takafuji M, Ishida M, Shiomi T,** et al. Development of a deep learning algorithm for detecting significant coronary artery stenosis in whole-heart coronary magnetic resonance angiography. J Cardiovasc Magn Reson. 2025;27(2):101932. doi: 10.1016/j.jocmr.2025.101932
80. **Galli M, Pereira NL, Lennon RJ,** et al. Genotype-Guided vs Conventional Oral P2Y12 Inhibitors in Acute Coronary Syndrome: A Combined Analysis of TAILOR-PCI and POPular Genetics. JACC Cardiovasc Interv. 2026 Feb 9;19(3):283-296. doi: 10.1016/j.jcin.2025.11.029
81. **Chen Q, Pan T, Wang YN,** et al. A Coronary CT Angiography Radiomics Model to Identify Vulnerable Plaque and Predict Cardiovascular Events. Radiology. 2023 Apr;307(2):e221693. doi: 10.1148/radiol.221693
82. **Li R, Wang M, Chen S, Zhang L.** Comparative efficacy and adherence of telehealth cardiac rehabilitation interventions for patients with cardiovascular disease: A systematic review and network meta-analysis. Int J Nurs Stud. 2024 Oct;158:104845. doi: 10.1016/j.ijnurstu.2024.104845
83. **Nabeta T, Bär S, Maaniitty T,** et al. Incremental value of a CCTA-derived AI-based ischemia algorithm over standard CCTA interpretation of predicting myocardial ischemia in patients with suspected coronary artery disease. J Cardiovasc Comput Tomogr. 2025 Nov-Dec;19(6):694-700. doi: 10.1016/j.jcct.2025.09.014
84. **Weir-McCall JR, Koweek L, Suchá D,** et al. Fractional flow reserve in coronary computed tomography angiography: An expert consensus document of the society of cardiovascular computed tomography (SCCT) and the society for cardiovascular angiography and interventions (SCAI). Endorsed by the American college of cardiology (ACC). J Cardiovasc Comput Tomogr. 2026 Jun 3;0(0). doi: 10.1016/j.jcct.2026.05.006
85. **Zhang W, Yin YB, Wang ZQ,** et al. Performance assessment of computed tomographic angiography fractional flow reserve using deep

learning: SMART trial summary. J Geriatr Cardiol JGC. 2025 Sep 28;22(9):793-801. doi: 10.26599/1671-5411.2025.09.002

86. **Andersen BK, Sejr-Hansen M, Maillard L,** et al. Quantitative flow ratio versus fractional flow reserve for coronary revascularisation guidance (FAVOR III Europe): a multicentre, randomised, non-inferiority trial. Lancet. 2024 Nov 9;404(10465):1835-1846. doi: 10.1016/S0140-6736(24)02175-5
87. **Xu B, Tu S, Song L,** et al. Angiographic quantitative flow ratio-guided coronary intervention (FAVOR III China): a multicentre, randomised, sham-controlled trial. Lancet. 2021 Dec 11;398(10317):2149-2159. doi: 10.1016/S0140-6736(21)02248-0
88. **Daemen J, van der Eijk JA, Barbierato M,** et al. Angiography-Based Physiology to Guide Coronary Revascularization. N Engl J Med. 2026 Jul 1;395(1):20-31. doi: 10.1056/NEJMoa2601841
89. **Woodward G, Bajre M, Bhattacharyya S,** et al. PROTEUS Study: A Prospective Randomized Controlled Trial Evaluating the Use of Artificial Intelligence in Stress Echocardiography. Am Heart J. 2023 Sep;263:123-132. doi: 10.1016/j.ahj.2023.05.003
90. **Narang A, Bae R, Hong H,** et al. Utility of a Deep-Learning Algorithm to Guide Novices to Acquire Echocardiograms for Limited Diagnostic Use. JAMA Cardiol. 2021 Jun 1;6(6):624-632. doi: 10.1001/jamacardio.2021.0185

TO CITE THIS ARTICLE:
Garg K, Bruich L, Enemark LJ, Sawalha K, Rana A, Agrawal A, Spraggins II RF, Khalaila O, Shehadeh M, Alhwarat B, Johnson C, Guha A, Zhang Y, Pontone G, Dani SS, Chindambaram V, Baskaran L, Tayal B, Al'Aref SJ. Artificial Intelligence in Coronary Artery Disease: From Detection to Precision Management. Methodist DeBakey Cardiovasc J. 2026;22(5):20-38. doi: 10.14797/mdcvj.1917

Submitted: 14 July 2026 **Accepted:** 14 September 2026 **Published:** 10 November 2026

COPYRIGHT:
© 2026 The Author(s). This is an open-access article distributed under the terms of the Attribution-NonCommercial 4.0 International (CC BY-NC 4.0), which permits unrestricted use, distribution, and reproduction in any noncommercial medium, provided the original author and source are credited. See https://creativecommons.org/licenses/by-nc/4.0/.

Methodist DeBakey Cardiovascular Journal is a peer-reviewed open access journal published by Houston Methodist DeBakey Heart & Vascular Center.