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LETTER TO THE EDITOR

From marginal gains to clinical utility: machine learning–based percutaneous coronary intervention risk prediction models

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Percutaneous coronary intervention (PCI) is one of the most frequently performed cardiovascular interventions,[1] yet post-procedural complications remain a concern, affecting up to 10% of patients.[2] While traditional risk assessment tools like the SYNTAX, GRACE, CathPCI bleeding, or NCDR AKI risk calculators have long guided clinicians in predicting procedural risks, artificial intelligence (AI)–enabled approaches to risk assessment can transform fixed statistical estimates into adaptive predictive strategies. The recent review by Zaka *et al.*[3] contributes to our understanding of AI-driven risk prediction models for PCI, highlighting their potential to improve predictive accuracy. Additional integration of multimodal data types and a transition to prospective trials involving AI-based PCI risk stratification tools could help bridge innovation to clinical utility.

Multimodal artificial intelligence approaches to percutaneous coronary intervention risk stratification

In the landscape of PCI risk stratification, pre-procedural and procedural variables represent complementary yet distinct domains of information, each providing unique insights into a patient's risk profile at a specific point along the clinical treatment pathway (*Figure 1*). Most published AI-based PCI risk stratification models use pre-procedural data, routinely available in electronic medical records (EMRs), such as demographic variables (i.e. age, sex, body mass index, blood pressure), comorbidities (i.e. diabetes, hypertension, chronic kidney disease), and laboratory parameters (i.e. creatinine, hemoglobin, troponins).[3,4] When deployed pre-interventionally, these models can strategically inform the selection of optimal interventional approaches, patient triage, and post-interventional care. Some of these models also incorporate echocardiography- and angiography-derived quantitative measurements—such as aortic valve area, lesion complexity, and stenosis severity—to develop a model using clinically relevant features.[3] Notably, no published models directly integrate echocardiography or angiography images in their raw form.

The methodological integration of data across modalities—including clinical variables, imaging, genetic markers, and social and environmental data—can aid in developing more comprehensive predictive models, termed multimodal AI models, which can realistically capture the complex multi-dimensional nature of available patient data that clinicians evaluate routinely. In precision healthcare, multimodal AI models have demonstrated significantly augmented predictive capabilities compared with unimodal models.[5] Therefore, it is likely that incorporating pre-operative imaging modalities like coronary angiography, cardiac computed tomography (CT) angiography, and cardiac magnetic resonance imaging will provide further insights, enhancing model performance and generating additional clinical value. Multimodal fusion of cardiac perfusion imaging with clinical data[6] and 12-lead electrocardiography signals with EMR data has enhanced predictive performance for personalized risk assessment,[7] positioning multimodal approaches as advantageous for improving risk prediction in PCI. However, multimodality is insufficiently investigated in PCI risk stratification, warranting further research and rigorous validation.

Risk stratification at key intervention timepoints

Accurate determination of input variables based on the intended time point at which the model will be deployed—pre-, intra-, or early post-PCI phases—is necessary for its adequate application and performance assessment. Variables like procedure duration or number of stents deployed are known predictors of outcomes following PCI but are highly dependent on pre-procedural variables like lesion complexity.[8] Artificial intelligence models comprising both pre- and intra-

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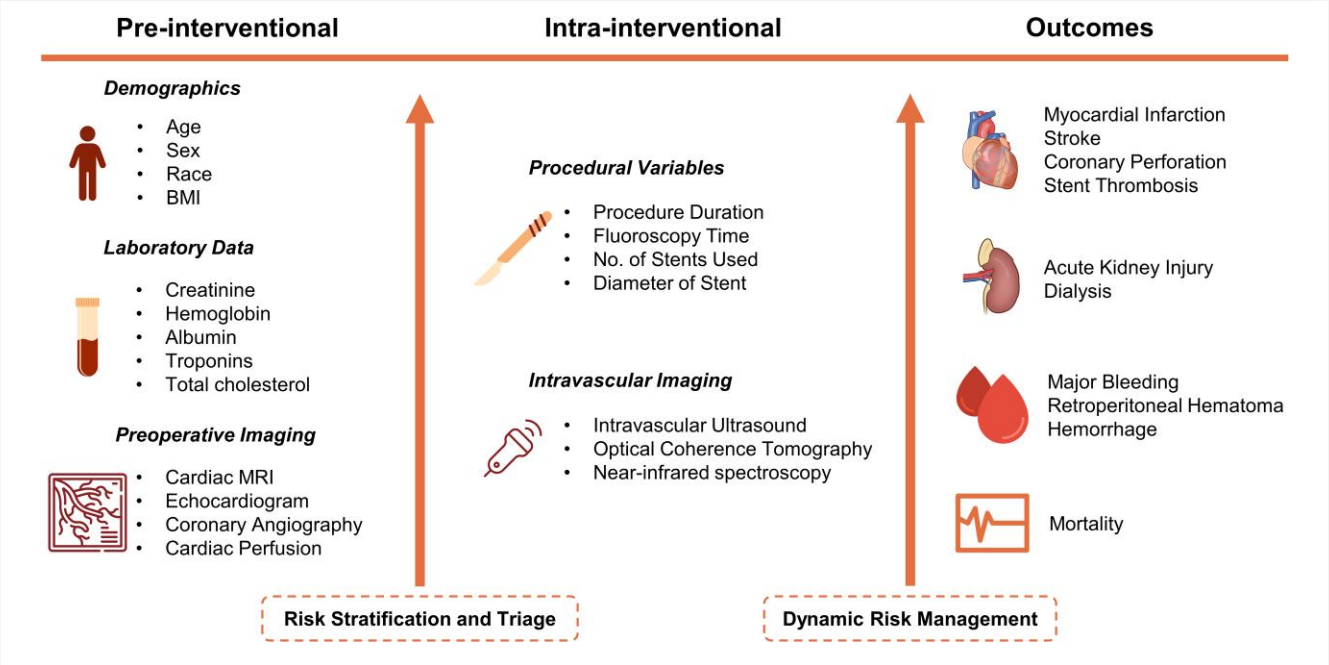

Figure 1 Input variables and prediction targets for multimodal machine learning approaches for risk stratification in patients undergoing percutaneous coronary interventions. Multimodal artificial intelligence models integrating demographic and laboratory data and pre-procedural imaging can be deployed at the pre-interventional stage to aid in patient risk stratification and triage. Models incorporating procedural variables and intra-vascular imaging can support dynamic risk management during percutaneous coronary intervention and facilitate the adaptation of post-interventional care based on individual complication risks.

Table 1 FDA-approved artificial intelligence/machine learning cardiovascular devices for risk assessment (January 2022 to December 2024)

Device	Class	Disease description	Prediction target	Predicate device
eCART	II	A cloud-based software device integrated with EMRs to anticipate clinical deterioration in adult ward patients	To predict the risk of patient deterioration (intensive care unit transfer or death)	CLEWICU
APPRAISE-HRI	II	An android application that uses vital sign data to stratify haemorrhage risk to aid clinical management and prioritize emergency care	To classify the risk of haemorrhage into low, average, or high	Analytic for Hemodynamic Instability (AHI)
CLEWICU System	II	A standalone software that calculates the likelihood of occurrence of certain clinically significant events for patients in critical care settings	To predict the likelihood of haemodynamic instability and to identify the patients at risk of deterioration	CLEWICU System (K200717)
SignalHF	II	A software that analyses physiological data from cardiac implants and personal health records to calculate the risk of heart failure	To predict the likelihood of heart failure within the next 30 days	Acumen™ Hypotension Prediction Index (HPI)
Cleerly ISCHEMIA	II	A software module to analyse coronary CT angiography images to indicate the presence or absence of coronary vessel ischaemia based on quantitative measures of atherosclerosis, stenosis, and vascular morphology	To predict the likelihood of coronary ischaemia, for improved detection of CAD	EchoGo Heart Failure
CorVista® system	II	A device to analyse physiological signals and provide reports indicating the likelihood of specific cardiac diseases at the point of care	To predict the likelihood of significant CAD in patients presenting with symptoms	Viz HCM

This table highlights the device class, description, prediction targets, and the predicate medical device that the approval process was based on. While these devices facilitate risk stratification in cardiac care, no device specifically addresses post-PCI risk prediction.
CAD, coronary artery disease.

procedural variables can be run towards the end of PCI or in the early post-interventional phase, where real-time data or variables like fluoroscopy time, lesion severity, or procedure duration become available. Therefore, these models may inform post-interventional risk for a specific patient and contribute valuable information for tailored clinical decision-making.

While incorporating procedural variables can augment the predictive accuracy of the models, having highly correlated features as input variables for the same model may induce redundancy and lead to statistical instability and reduced model performance. It is conceivable that, given this interdependence, developing a model using pre-interventional variables and imaging may suffice as the most or equally informative and definitive approach.

The use of intra-vascular imaging (intra-vascular ultrasound, optical coherence tomography, near-infrared spectroscopy) during PCI has been shown to reduce the rate of major adverse cardiac events.[9] Hence, a multimodal machine learning (ML) model integrating intra-vascular imaging with other (pre-)procedural variables could potentially offer a novel approach towards enhanced procedural precision, real-time risk assessment, and dynamic risk management (*Figure 1*).

Translational and regulatory approval pathways

Despite their demonstrated performance,[3] computational post-PCI complication prediction models are not yet available at the point of care. This under-utilization stems broadly from the paucity of universally accepted standards and guidelines for integrating AI-based decision support systems into clinical practice.

From January 1, 2022 to December 1, 2024, 48 artificial AI/ML-enabled medical devices were approved by the Food and Drug Administration (FDA) in the field of cardiovascular care. A total of 12 of these devices facilitate cardiac risk prediction, a representative sample of which is presented in *Table 1*. These devices are predominantly approved within the FDA 510(k) clearance process, the most common approval pathway for medical devices in the United States, and address narrowly defined clinical use cases such as the likelihood of heart failure. None of these devices facilitate pre-interventional or early post-interventional stratification of complications after PCI (*Table 1*). Besides, with only a handful of clinical trials either ongoing or completed (ClinicalTrials.gov; search: other terms: Machine Learning, Intervention: Percutaneous Coronary Intervention, PCI; date: 4 December 2024), a considerable gap exists between retrospectively developed models and their prospective clinical evaluation and external validation. Addressing this gap would lead to better overall performance and generalizability of the resulting models, as these diverse cohorts will better represent the heterogeneity in patients undergoing PCI. Additionally, benchmarking against current standards of care for complication risk stratification, such as the SYNTAX, GRACE, CathPCI bleeding, or NCDR AKI risk calculators, will facilitate a meaningful evaluation of the clinical benefit of AI-based risk stratification models.

Percutaneous coronary intervention risk stratification is a complex application that extends beyond descriptive tasks and influences clinical decision-making and treatment planning in a high-risk domain. This intricacy makes translation into clinical settings particularly challenging. Presently, PCI risk stratification is in its infancy in terms of clinical translation and regulatory approval. However, with a concerted focus on harmonizing regulatory frameworks and establishing clinically oriented performance standards for AI, we can propel its adoption in the high-stakes domain of cardiac care.

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