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REVIEW

Machine Learning in Invasive and Noninvasive Coronary Angiography

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Abstract

Purpose of Review The objective of this review is to shed light on the transformative potential of machine learning (ML) in coronary angiography. We aim to understand existing developments in using ML for coronary angiography and discuss broader implications for the future of coronary angiography and cardiovascular medicine.

Recent Findings The developments in invasive and noninvasive imaging have revolutionized diagnosis and treatment of coronary artery disease (CAD). However, CAD remains underdiagnosed and undertreated. ML has emerged as a powerful tool to further improve image analysis, hemodynamic assessment, lesion detection, and predictive modeling. These advancements have enabled more accurate identification of CAD, streamlined workflows, reduced the need for invasive diagnostic procedures, and improved the diagnostic value of invasive procedures when they are needed. Further integration of ML with coronary angiography will advance the prevention, diagnosis, and treatment of CAD.

Summary The integration of ML with coronary angiography is ushering in a new era in cardiovascular medicine. We highlight five use cases to leverage ML in coronary angiography: (1) improvement of quality and efficacy, (2) characterization of plaque, (3) hemodynamic assessment, (4) prediction of future outcomes, and (5) diagnosis of non-atherosclerotic coronary disease.

Keywords Machine learning · Coronary computed tomography angiography · Invasive coronary angiography

Introduction

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality despite remarkable advances in invasive and noninvasive diagnostic modalities [1]. A comprehensive evaluation of CAD involves assessing the severity, burden, and characteristics of coronary atherosclerosis, with (i) noninvasive modalities such as computed coronary tomography angiography (CCTA) and/or (ii) catheterization with invasive coronary angiography (ICA) and sometimes intravascular imaging. A comprehensive understanding of CAD requires not only an identification of its presence but also an assessment of the coronary burden which represents the extent and severity of coronary atherosclerosis. Furthermore, the specific characteristics of plaques, such as their composition, vulnerability to rupture, and location, play crucial roles in translating to different clinical outcomes. Characterization of plaque burden and features might lead to potential therapeutic nuances and variability in prognostication [2]. In addition to this anatomic evaluation of CAD, a physiologic evaluation of the flow-limiting effects of a stenosis in a coronary artery is often necessary and constitutes the main driver for revascularization decisions. Physiologic evaluations can also be performed (i) noninvasively such as with myocardial perfusion stress testing and fractional flow reserve-computed tomography (FFR-CT) or (ii) invasively using pressure-wire indices such as fractional flow reserve (FFR) or non-hyperemic pressure wave ratios (iFR, DFR, RFR, etc.) [3–5].

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Although CCTA and ICA lie on different ends of the invasiveness spectrum, they are the two most important modalities for anatomic evaluation of CAD. As a noninvasive option, CCTA offers visualization of coronary tree and atherosclerotic plaques but also can accurately quantify plaque volumes and identify high-risk plaque features such as low attenuation plaque and napkin-ring sign that have been associated with future cardiovascular events [6, 7]. On the other hand, ICA not only can assess coronary anatomy and plaque and identify plaque characteristics with intraluminal imaging, but also can facilitate real-time therapeutic interventions [6].

The proliferation of artificial intelligence (AI)-enabled medical technologies in recent years has led to new capabilities of diagnostic and therapeutic modalities. Historically, medical procedures and diagnostics relied on a blend of practitioner expertise and available technological tools. However, AI has bridged the gap between massive datasets and actionable insights, processing and analyzing intricate data at unprecedented scales [8]. Unsurprisingly, this progress was also represented in the realm of cardiology. The diagnostic nuances and treatment intricacies required in cardiology often mandate processing vast arrays of data, from electrocardiograms to imaging modalities. Therefore, AI found many potential use cases to improve diagnostics and therapeutics by identifying patterns and anomalies that might otherwise escape the human eye [8].

The Need to Improve CCTA and ICA

The developments in noninvasive imaging, particularly CCTA, as well as advancements in invasive intraluminal imaging have ushered in a revolutionary era for visualizing coronary anatomy and plaques but most importantly identifying plaque characteristics [9]. However, despite these advancements, coronary disease remains underdiagnosed and undertreated leading to significant morbidity and mortality in the world [10].

There are several issues with the current diagnostic tools including inter-reader variability, insufficient accuracy, and high costs (Table 1) [11•, 12]. One of the primary concerns is the subjectivity that comes with interpreting CCTA and ICA. As the interpretations of the images largely depend on the expertise and experience of the radiologist or cardiologist, there is an inherent variability in readings [11•]. Two clinicians may perceive the severity of a stenosis differently or might miss a subtle lesion altogether. This lack of standardization can potentially lead to misdiagnosis, unnecessary interventions, or overlooked therapeutic opportunities [12].

Despite the high-resolution imaging provided by CCTA and ICA, there are three major limitations when it comes to their accuracy. First, the presence of heavy calcifications can pose challenges in determining the exact extent of luminal narrowing, leading to either overestimation or underestimation of stenosis [9]. Second, while invasive angiograms provide a two-dimensional view, they might not capture the complexities of certain lesions, particularly in tortuous coronary segments unless intraluminal imaging is utilized. Third, these advanced imaging modalities can be costly and might not be readily available in all healthcare settings, especially in low-resource areas [13].Considering these challenges, there is an impending need to refine current diagnostic strategies. The integration of machine learning (ML) could offer solutions by providing a more standardized, accurate, and comprehensive analysis of coronary artery disease and lower associated costs. However, despite advancements in medicine, cardiology, and imaging, ML has not yet well penetrated the coronary angiography space.

ML has already made significant strides in medical imaging across various specialties. In pathology, ML has been employed to analyze digital pathology slides, aiding in the detection and classification of diseases such as malignancies [14]. Stroke detection has been revolutionized with algorithms that rapidly identify signs in CT scans, specifically targeting large vessel occlusions [15, 16]. In dermatology and ophthalmology, ML-enabled tools can assist in diagnosing conditions such as skin cancers [17] and diabetic retinopathy [18]. Similarly, ML has the potential to significantly enhance coronary angiography. It can improve image interpretation by detecting subtle atherosclerotic disease and provide more information on plaque morphology

Table 1 Major Issues with CCTA and ICA and potential ML solutions

Problem	Subsequent harm	ML solution
Inter-reader variability	• Misdiagnosis • Unnecessary interventions • Overlooked therapeutic opportunities	• Automatization and standardization of interpretations for excellent reproducibility
Insufficient accuracy	• Over- or under-estimation of stenosis	• Decrease imaging artifacts and increase accuracy
High costs	• Increased healthcare expenditure • Limited accessibility	• Reduce costs by increasing efficiency and reducing operating time

CCTA coronary computed tomography angiography; *ICA* invasive coronary angiography; *ML* machine learning and hemodynamic significance, reduce radiation exposure through optimized parameters, and offer predictive insights by analyzing angiographic data alongside patient history. Furthermore, ML can automate intricate measurements, ensuring consistency and reducing variability, while also integrating angiographic data with other diagnostic modalities for a holistic view of cardiovascular health.

We have identified five key areas of opportunity to leverage ML in coronary angiography to advance the prevention, diagnosis, and treatment of CAD (Fig. 1).

Improvement in Quality and Efficacy of Coronary Evaluation

ML algorithms, especially those based on deep learning architectures, have shown remarkable proficiency in image recognition tasks [19]. When trained on vast datasets of angiograms, these algorithms have the potential to achieve a level of precision that might rival or even surpass, medical experts. There are three primary advantages of ML in this context. First, ML can identify and quantify features such as stenoses, plaques, and vessel diameters with high accuracy [20, 21••]. Conventional manual analysis is often subjective and prone to variability between different observers [12]. ML on the other hand might offer a consistent and objective analysis, significantly reducing human error [20, 21••], similar to prior studies on echocardiograms [22]. Second, the subtleties in angiographic images, which might be missed during manual inspection, can be detected by ML algorithms. These subtle findings, though they might appear insignificant, can often be clinically relevant and indicative of early disease stages or potential complications. By ensuring that such findings are not overlooked, ML can aid in enhancing the overall diagnostic quality. Third, automated image analysis can streamline diagnostic workflows. Manual analysis of angiograms can be time-consuming, especially in complex cases. ML-enabled tools can rapidly process these images, providing insights in a fraction of the time. This acceleration in the diagnostic process allows for faster patient management decisions, potentially leading to timely interventions and improved patient outcomes [23].

The clarity and quality of angiographic images are paramount for accurate diagnosis. With the advent of ML, there is an opportunity to significantly refine these images. In other cardiovascular imaging modalities, ML algorithms, particularly those based on convolutional neural networks, have demonstrated the ability to filter out noise and artifacts,

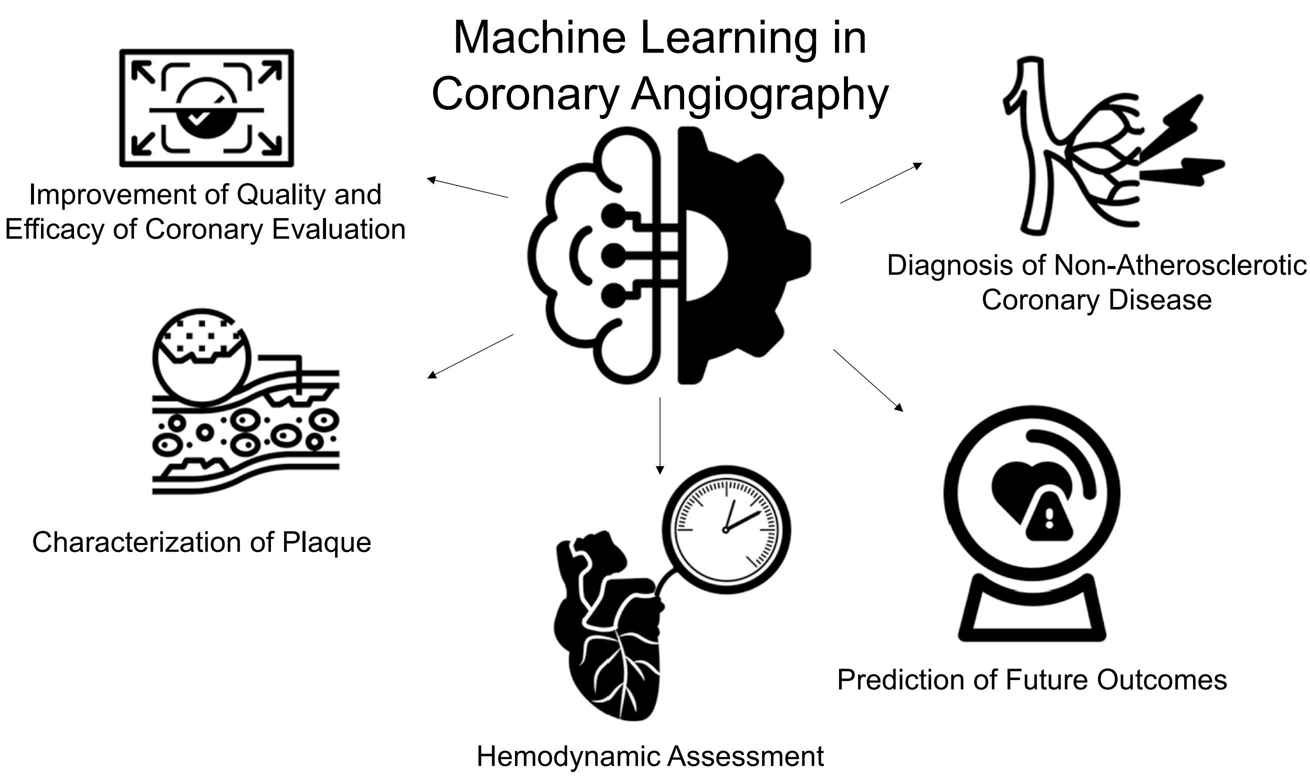

Fig. 1 Five key areas of opportunity to leverage ML in coronary angiography. ML offers significant potential in coronary angiography, particularly in five key areas to enhance the prevention, diagnosis, and treatment of CAD: (1) improvement of quality and efficacy; (2) characterization of plaque; (3) hemodynamic assessment; (4) prediction of future outcomes; and (5) diagnosis of non-atherosclerotic coronary disease

enhancing the overall clarity of the images [21••, 24]. Additionally, these algorithms can enhance contrast, making it easier to differentiate between various structures and abnormalities in the coronary arteries. As a result, even miniscule changes or abnormalities, which might be overlooked in conventional image interpretation, become discernible [25].

Enhanced images are especially beneficial in challenging cases, where traditional imaging might fall short due to factors like patient movement, suboptimal contrast injection, or anatomical complexities. In such scenarios, the capabilities of ML can be harnessed to improve image quality, ensuring that the diagnosis is based on the best possible visualization of the coronary anatomy. Although this remains to be studied, ML-enhanced imaging and improved image quality could potentially result in more accurate diagnoses, timely interventions, and ultimately, better patient outcomes. In a recent example from multi-modal magnetic resonance imaging, using a cascade of convolutional neural networks for brain tumor segmentation led to an improvement of segmentation accuracy [26].

Characterization of Coronary Plaque

CCTA is a powerful noninvasive tool to visualize coronary anatomy and most importantly, coronary plaque morphology [9]. Its ability to provide high-resolution images of the coronary arteries noninvasively makes it invaluable for detecting and characterizing coronary artery disease. In contrast, ICA primarily offers an anatomical assessment of the coronary arteries. It visualizes the lumen of the arteries and the extent of the coronary disease highlighting areas of potential significant flow restriction, which can be indicative of clinically significant stenoses [27]. However, it also allows for intravascular coronary imaging which provides excellent detail and a granular morphological understanding of plaques. Techniques such as optical coherence tomography (OCT) and intravascular ultrasound (IVUS) provide high-resolution images of plaque composition, size, and location. These modalities delve deeper into the vessel wall, revealing details that are often invisible to other imaging techniques, thus providing invaluable information for planning interventional strategies [28]. This information offers insights into plaque composition, stability, and potential for rupture [29]. With the integration of ML algorithms, these imaging techniques can be further enhanced by analyzing the vast amount of data generated by these modalities, offering predictive insights that can help clinicians anticipate potential complications like plaque rupture or thrombosis [30]. By understanding the biological characteristics of plaques, clinicians can tailor treatment strategies. This personalized approach, ranging from medication adjustments to specific interventional procedures, ensures that patients receive optimal care based on their unique plaque biology [31]. Furthermore, these algorithms can integrate data from multiple sources, such as patient history, blood tests, and other diagnostic tests, to provide a comprehensive risk profile for individual patients [32]. With this knowledge, one can devise more personalized treatment strategies. For some patients, this might lead to medication adjustments and optimization, while for others, it can involve percutaneous coronary interventions such as stenting or balloon angioplasty [33]. This personalized approach might ensure that patients receive optimal care tailored to their unique plaque biology and overall cardiovascular risk, leading to better outcomes [34].

Hemodynamic Assessment of Coronary Stenosis

Both CCTA and ICA can provide information on lesion location, severity, and extent. However, ICA provides an additional advantage by allowing hemodynamic evaluation of potentially clinically significant lesions. Hemodynamic evaluation can be done using FFR, a measure that compares the pressure before and after the stenosis under maximal hyperemia [35] or instantaneous wave-free ratio (IFR) that achieves the same by evaluating wave-free period of cardiac cycle without the need for drug-induced hyperemia [3]. Recently, noninvasive methods like CT-derived FFR have emerged as reliable alternatives to invasive FFR measurements [5]. CT-derived FFR, which utilizes computational fluid dynamics on CCTA data, offers the advantage of assessing both anatomical and functional significance of coronary lesions without the need for invasive catheterization [4]. HeartFlow, a specific CT-derived FFR analysis tool, has been shown to improve diagnostic accuracy and patient outcomes while potentially reducing healthcare costs [36].

Despite the advancements in CT-derived FFR technology, ICA still offers a benefit by allowing for interventions during the same procedure if the lesion of interest is deemed to be hemodynamically significant. However, invasive hemodynamic assessment requires passing a coronary wire through the lesion in the coronary artery which is a further invasive method that increases time and potential risks associated with the procedure [3]. Deep learning models trained with datasets with hemodynamic measurements and high-quality angiograms have the potential to provide the same hemodynamic information without the need for coronary wiring [37, 38]. This technology could enhance the evaluation of flow characteristics in lesions that were not initially identified as intermediate through visual assessment. This advancement offers an additional avenue to reduce oversight by standardizing measurements.

Prediction of Future Outcomes

Despite our growing knowledge and advanced diagnostic tools, recurrent cardiovascular events remain a significant concern [2]. This underscores the need for risk stratification based on improved prediction models and personalized preventative interventions. The coronary artery calcium (CAC) score, derived from non-contrast CT scans, has been a cornerstone in predicting future cardiovascular events [39]. It quantifies the amount of calcium in coronary arteries, providing insights into the extent of atherosclerotic plaque burden. While the CAC score has proven to be highly beneficial, it can only identify calcified plaques and cannot predict future events based on plaques morphology. This especially poses a potential issue for the younger population with higher likelihood of having noncalcified coronary plaques [40]. Therefore, advanced modalities like CCTA and ICA combined with ML could offer insights beyond calcification, such as plaque morphology, and inflammation. It holds promise in enhancing our predictive capabilities and reducing recurrent events by analyzing the vast patient data outside of a given imaging modality and identify subtle patterns [19]. Furthermore, ML can also be used to enhance existing predictive tools such as CAC score by incorporating clinical features and improving quantification of CAC scoring [41•].

Diagnosing Non-atherosclerotic Coronary Disease

While atherosclerosis remains at the forefront of concerns in coronary artery disease, there are non-atherosclerotic conditions that demand equal attention and understanding. Spontaneous coronary artery dissection (SCAD), cardiac allograft vasculopathy (CAV), and microvascular disease are among these conditions, each presenting its own set of challenges and complexities (Table 2).

Spontaneous coronary artery dissection is characterized by a spontaneous tear in the coronary artery wall leading to a false lumen, which can lead to myocardial ischemia and infarction. SCAD is an uncommon yet critical cause of acute coronary syndrome, particularly among younger individuals and women [42]. The exact etiology of SCAD remains to be fully elucidated, but it has been associated with a variety of conditions that affect hormonal, shear stress, and vascular structural factors [43]. CCTA and ICA with intravascular ultrasound are commonly employed tools for its identification [44] but diagnosis can be challenging due to its atypical presentation and variable imaging findings [44]. ML-enhanced imaging interpretation has the potential to improve diagnosis of SCAD by increasing accuracy of reads and reducing missingness.

Cardiac allograft vasculopathy (CAV) is a unique and progressive form of coronary artery disease that affects heart transplant recipients [45]. It is characterized by diffuse intimal thickening and fibroproliferation, leading to stenosis of the coronary arteries. CAV is one of the leading causes of late graft failure and mortality post-heart transplantation. Traditional diagnostic methods, such as coronary angiography, may not be sensitive enough to detect early changes of CAV, given its diffuse nature [46]. Similar to CAV, microvascular disease pertains to the dysfunction of the coronary microvasculature and affects the microcirculation due to factors that are traditionally associated with coronary disease such as hypertension, hyperlipidemia, and diabetes or endothelial dysfunction [47]. It can potentially lead to symptoms such as angina despite the absence of significant epicardial coronary artery stenosis [48]. The intricate nature of these conditions, combined with their diverse presentations, means that they often elude conventional diagnostic tools and strategies, leading to underdiagnosis or misdiagnosis. A variety of invasive and noninvasive imaging modalities are used to assess microvascular dysfunction that utilizes

Table 2 Challenges with and potential solutions for non-atherosclerotic coronary disease

Disease	Problem	Potential ML solution
Spontaneous coronary artery dissection	• Atypical presentation • Variable imaging findings	• Increased accuracy • Reduced missingness
Cardiac allograft vasculopathy	• CCTA and ICA not sensitive to detect early changes • Diverse presentations • Variable specificity and sensitivity of noninvasive imaging modalities • Gold standard is invasive	• Detection of vasculopathy without the need for pressure wires
Microvascular disease	• Variable specificity and sensitivity of noninvasive imaging modalities • Invasive measurement associated with cost and risk	• Detection of microvascular disease without the need for pressure wires

CCTA coronary computed tomography angiography; *ICA* invasive coronary angiography; *ML* machine learning indices such as coronary flow reserves (CFR) and index of microcirculatory resistance (IMR) [49]. However, each noninvasive imaging modality has specific challenges and various sensitivity and specificity levels for detecting microvascular dysfunction [49]. Invasive measurements are the gold standard to diagnose microvascular disease; however, they require advancing pressure wires through coronary arteries which increase procedural risks and time spent during the procedure [49, 50]. Similar to the technologies developed to measure FFR and IFR based on invasive and noninvasive coronary angiograms using flow dynamics, ML algorithms can help with the assessment of coronary microvasculature without the need for pressure wires.

Challenges with Using ML in Coronary Angiograms and Potential Solutions

ML applications in coronary angiograms present both opportunities and challenges. The most important considerations and challenges when using ML applications in coronary angiograms are (i) variability of findings between patients, (ii) ethical considerations, (iii) data privacy, and (iv) interpretability. First, the nature of coronary artery lesions, combined with the variability in patient anatomy and the subtle distinctions between pathological and normal findings, can make automated analysis complex. However, advancements in ML algorithms and the increasing availability of labeled datasets are addressing these complexities [51]. For instance, the variability in coronary angiogram images, stemming from differences in equipment, techniques, and patient anatomy, can be mitigated by training ML models on diverse and representative datasets. Additionally, advanced preprocessing techniques and data augmentation can help filter out noise and artifacts, ensuring that ML models are trained on high-quality data [24].

Second, ethical considerations are paramount when integrating ML into medical imaging. Ensuring patient privacy is crucial, and data used for training ML models must be anonymized, removing any personally identifiable information [52]. Moreover, the potential for algorithmic bias, where models might perform differently for various patient subgroups, is a concern that needs proactive addressing to ensure equitable care. Transparency in communicating to patients about how their data will be used and obtaining informed consent is also important. Furthermore, ML models should be regularly evaluated and updated to ensure they are free from biases and provide consistent results across diverse patient groups.

Third, data sharing is another challenge that needs close attention. While ML models require vast amounts of data to achieve high accuracy, sharing patient data across institutions raises concerns about data privacy and security. Innovative solutions like federated learning, where the model is trained across multiple sites without sharing raw data, are emerging [53]. Ensuring data encryption and implementing differential privacy techniques can further safeguard patient information.

Finally, a significant criticism of ML, especially deep learning models, is their “black box” nature [54]. The challenge lies in understanding how these models arrive at their decisions, a crucial aspect in medical applications where interpretability is essential. Emphasis should be placed on developing or using ML models that offer insights into their decision-making processes. Interpretation and data visualization methods such as saliency maps [55], gradient-weighted class-activation maps [56], backward optimization [57], and novelty detection [58, 59] can help visualize which parts of angiograms were most influential in the model’s decision, adding a layer of transparency.

Conclusion

Diagnosis of CAD requires assessing the severity and characteristics of coronary atherosclerosis, with both CCTA and ICA playing pivotal roles in diagnosing and offering insights into plaque characteristics. Following the growth of AI-enabled technologies in other areas of medicine, ML can similarly be leveraged to enhance both invasive and noninvasive coronary angiography for better diagnosis and management of CAD. We highlighted five potential use cases in which ML for coronary angiography holds significant promise: (1) improvement of quality and efficacy, (2) characterization of plaque, (3) hemodynamic assessment, (4) prediction of future outcomes, and (5) diagnosis of non-atherosclerotic coronary disease. While ML offers transformative potential in the realm of coronary angiograms, careful consideration of challenges, ethical implications, data sharing protocols, and model interpretability is essential to harness its full potential and ensure optimal patient care.

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Declarations

Competing interests The authors declare no competing interests.

Conflict of Interest Dr. Fahed reports being co-founder of Goodpath and received a research grant from Abbott Vascular, unrelated to the subject of this manuscript. Dr. Unlu has nothing to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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•• Of major importance

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