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Artificial Intelligence in Coronary Artery Disease: Essential Aspects

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ABSTRACT

Coronary artery disease (CAD) remains the predominant cause of death in the world, especially in western countries. Through technological breakthroughs in recent years, artificial intelligence (AI) is increasingly being applied in the field of cardiovascular medicine for the interpretation of invasive imaging diagnostic techniques such as coronary angiography (CA) and non-invasive techniques, coronary CT angiography (CCTA) being implemented to guide subsequent management of CAD patients. The present aim is to review published data in medical literature to analyze the current use of AI in CAD patients.

KEYWORDS Artificial intelligence; coronary artery disease; prognosis

INTRODUCTION

Coronary artery disease (CAD) remains the predominant global cause of human diseases, accounting for >9 million deaths in 2016, according to the World Health Organization (WHO) estimates, especially in western countries [1]. In recent years, in order to increase the efficacy in the diagnosis and management of CAD, artificial intelligence (AI) is being increasingly applied for the interpretation of invasive imaging diagnostic techniques such as coronary angiography (CA) and non-invasive techniques, including coronary CT angiography (CCTA) [2], [3]. This increasing use of AI in CAD patients is also a result of new indications for imaging in the 2021 American College of Cardiology/American Heart Association Chest Pain Guideline with Class I recommendation for either invasive and non-invasive imaging in patients with acute and stable chest pain at intermediate risk patients [4]. Between 2001 and 2020, the proportion of AI/ML-related articles in major cardiology journals per month was 0.4% as compared to 17.8% per month by 2021. The goal of this review is to analyze the current use of AI in the diagnosis and management of CAD patients.

ARTIFICIAL INTELLIGENCE IN CAD PATIENTS: ESSENTIAL ASPECTS

AI can be practically defined as a subset of computer science dedicated to creating systems, algorithms, or models that can perform tasks in place of the traditional manual method (Figure 1). Currently, two different subsets of AI can be identified: the former is represented by machine learning (ML) while the latter by deep learning (DL). ML can be further subdivided into supervised learning, unsupervised learning, semi-supervised learning, and reinforcement learning [5]. In CAD patients, the most applied practices are supervised learning and unsupervised learning. Specifically, supervised learning categorizes data that is subsequently used to classify unseen data. For example, this approach can be adopted to predict a patient's response to certain treatments [6]. Conversely, unsupervised learning algorithms are trained to find patterns or conclusions through unlabeled training data. An example of unsupervised learning in CAD patients can be represented by identifying distinct clinical subgroups of patients which may benefit from targeted therapy. The second main subset of AI is represented by ML, which is mainly based on regression models, random forests (RF), and support vector machines (SVM) [7]. In CAD patients specifically, regression approaches are generally adopted for classification tasks. In CAD and other cases, both the diagnosis and prognosis prediction depend on many risk factors, which may lead to overfitting. To overcome this problem, the use of RF, which can be defined as a combination, or better, integration of decision trees where each model relies on the values of a random vector that is sampled independently and

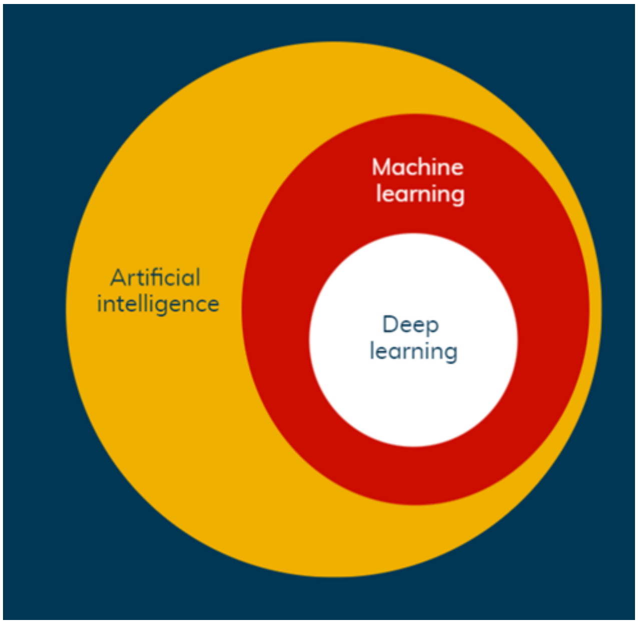

FIGURE 1. **Basics of artificial intelligence (AI), machine learning (ML), and deep learning (DL).** AI refers to the use of computational techniques to perform tasks characteristic of human intelligence. Conversely, ML represents a subfield of AI that enables computers to learn automatically by being exposed to large amounts of data. DL is a specific form of ML that uses multilayered artificial neural networks to elaborate predictions directly from input data.

with equal distribution for all decision trees in the "forest". These approaches can be adopted to identify new imaging biomarkers and/or integrate data from many different sources to provide patient-tailored risk prediction through anatomic and functional imaging assessment of CAD.

TECHNICAL ASPECTS OF AI FOR CAD PATIENTS

The use of AI in CAD patients assumes that a basic CA has been performed using a standard technique evaluating several parameters, such as the coronary flow (Thrombolysis in Myocardial Infarction (TIMI) flow), lesion severity (in terms of both percentages of stenosis and length), location of the lesion, presence of collateral vessels, identification of thrombi, calcification and congenital abnormalities. Subsequently, the acquired frames must be transformed into three-dimensional structures using segmentation techniques and dedicated protocols for the reconstruction of the real anatomy [8]. Conventionally, the frame used for the analysis is generally captured during the end-diastolic phase of the cardiac cycle to minimize coronary artery motion and limit artifacts. Segmentation can be performed either manually or using automated image analysis, which uses trained DL algorithms to automatically segment coronary arteries in coronary angiography [9], [10]. These approaches have differing accuracy, as shown in Table 1.

TABLE 1. **Studies analyzing artificial intelligence for automated coronary angiography imaging analysis.** (ACC: accuracy, AUC: area under curve, F1: F1 score, SE: sensitivity)

Authors	Year	Type of analysis	Performance
Du T et al. [10]	2021	Segmentation	ACC:98% SE: 85%
Zhao C et al. [11]	2021	Segmentation	DSC: 0.89
Moon JH et al. [12]	2021	Lesion detection and classification	AUC: 0.96
Danilov VV et al. [13]	2021	Lesion detection and classification	F1: 0.96
Pang K et al. [14]	2021	Lesion detection and localization	F1: 0.88
Chen S et al. [15]	2020	Lesion detection and classification	F1:0.91 to 0.97
Wu W et al. [9]	2020	Lesion detection	F1: 0.83

CURRENT USE OF ARTIFICIAL INTELLIGENCE IN CAD PATIENTS

Fractional flow reserve

AI is currently adopted for several purposes in CAD patients. For example, one of the main uses is the functional evaluation of coronary artery blood flow, which represents the main aspect that guides treatment decisions [16]. Fractional flow reserve (FFR) remains the most used metric. From a physical point of view, FFR evaluates the mean distal coronary pressure divided by the mean proximal pressure during maximal hyperemia [17]. However, this type of evaluation presents some limitations, represented by the invasive assessment, the need for costly pressure wires, and a prolonged procedural time [18], [19]. Therefore, in order to overcome these limitations, some interventionalists use the so-called quantitative flow ratio (QFR), which is a non-invasive method used to calculate functional sufficiency based on 3D-angiographic reconstruction and computational fluid dynamics [20]. Unfortunately, as of current QFR analysis is not readily available for daily clinical practice at the catheterization laboratory and requires expensive computational post-processing. AI-based FFR estimation requires less processing time as compared to QFR estimation based on computational fluid dynamics [21]. Similarly, a new software called AutocathFFR has demonstrated the ability to detect coronary lesions and predict their FFR value without coronary artery annotation or view selection with a sensitivity, specificity, positive predictive value, and negative predictive value of 0.88, 0.93, 0.94, and 0.87, respectively [18].

Coronary Calcium score

Coronary artery calcium (CAC) represents a marker of coronary atherosclerosis and a powerful predictor of angiographically significant obstructive CAD [22]. Nowadays, CAC scoring obtained from non-contrast electrocardiographically gated cardiac CT requires manual interaction by an operator. Conversely, ML approaches and analysis may allow rapid and automated quantification of CAC. Available data indicate that fully automated ML- and DL-based quantification of CAC are feasible and reliable compared with manual measurements [23], [24].

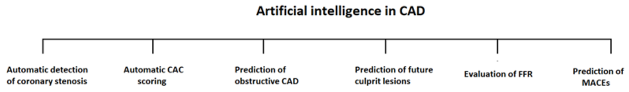

FIGURE 2. Overview of artificial intelligence application in patients with coronary artery disease.

Coronary artery stenosis

Several previous large investigations have already demonstrated the prognostic value of anatomic assessment of CAD with coronary CCTA [25]. Several AI approaches have been evaluated to automatically determine the degree of coronary stenosis directly from image data achieving a sensitivity of 95% and specificity of 67% compared with human operators. Furthermore, CCTA-derived measures of coronary stenosis have also been integrated into ML models for outcome prediction demonstrating good performances [25]-[28].

Coronary Plaque Characterization

In current clinical practice, CCTA allows the assessment of plaque morphology, as well as the presence of positive remodeling, spotty calcification, or napkin-ring sign, which have demonstrated a significant predictive value for future acute coronary syndrome [28], [29]. CCTA-derived quantitative plaque measures have also been incorporated into different ML models over the years to enhance outcome prediction demonstrating a superior performance compared with quantitative plaque features or qualitative high-risk plaque features alone [30]. Moreover, ML models provided superior prediction for lesion-specific ischemia when compared to stenosis severity or pretest probability of CAD [31].

FUTURE PERSPECTIVES

Undoubtedly, AI will be a useful tool in the management of CAD patients. However, a problem to be considered due to this would be the rise of clinicians who may always accept a prognosis obtained through ML, which may influence the lives of patients. Secondly, the absence of adequate knowledge of the use of AI in CAD patients, compounded with the absence of adequate training/knowledge regarding the basic process underlying this type of analysis may limit the diffusion of such techniques. Similarly, the absence of large datasets to train and validate AI modes may lead to poor performance of AI in uncommon diseases [32]. Conversely, it is also true that cardiovascular data needed for AI analysis are widely available in daily clinical practice (such as medical imaging, blood sample, and electronic health records); these aspects may facilitate the adoption of ML. It is important to note, however, that to date, unsupervised learning methods have rarely been adopted in the field of cardiac imaging. It should also be noted that misdiagnosis or missed diagnosis, system error, and unrepeatable results may also occur using AI-related software. Therefore, clinicians cannot be replaced by AI since they remain fundamental in judging the AI results, and considering the specific conditions of the patient, and incorporating their own experience in every scenario.

CONFLICTS OF INTEREST

None of the authors have conflicts of interest to declare

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