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Artificial intelligence and machine learning in cardiovascular computed tomography

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Abstract

Computed tomography (CT) is emerging as a prominent diagnostic modality in the field of cardiovascular imaging. Artificial intelligence (AI) is making significant strides in the field of information technology, the commercial industry, and health care. Machine learning (ML), a branch of AI, can optimize the performance of CT and augment the assessment of coronary artery disease. These ML platforms can automate multiple tasks, perform calculations, and integrate information from a variety of data sources. In this review article, we explore the ML in CT imaging.

Key Words: Computed tomography; Machine learning; Artificial intelligence; Cardiovascular imaging

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Core Tip: Machine learning (ML), a subset of artificial intelligence, contains multiple algorithms which include supervised, unsupervised, reinforcement and deep learning. These algorithms can greatly augment multiple aspects in computed tomography which

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include automated segmentation, diagnosis, and stratification based on risk. Outputs need to be carefully assessed by the medical team for any potential biases. For the future of computed tomography and cardiovascular imaging, ML algorithms need to be integrated in clinical care.

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INTRODUCTION

In this digital era, distance is no longer a limiting factor and information is emanating from a variety of devices and sources[1]. These technological innovations have considerably transformed our perception, culture, and our daily lifestyles[2]. Similarly, many of these changes have trickled downwards in healthcare and are especially apparent in the field of cardiovascular imaging. Over the last 10 years, the field of computed tomography (CT) has expanded tremendously with significant changes in diagnostic performance and prognostic implications in coronary artery disease[3,4]. Coronary CT angiography (CTA) is now heralded as an established diagnostic modality in the evaluation of coronary artery disease (CAD)[4,5]. With each year, data arising from each imaging scan is increasing exponentially in intricacy and size[6]. As we approach this technological ceiling, the sheer complexity of this information will supersede the analytic capabilities of conventional statistical software[7].

Artificial Intelligence (AI) refers to a set of actions that can mimic human cognitive thinking and decision making[8]. Machine learning (ML), a branch of AI, can extrapolate hidden characteristics or relationships present in vast expanses of data[2]. It can analyze data from a multitude of sources and link the information in user-friendly approaches[9]. In addition, it can automate several processes and perform many calculations[10]. With the application of ML algorithms in CT for cardiology, it can elevate the modality to unprecedented new heights which can improve the quality of patient care. In our review, we evaluate recent advances and progression of ML in cardiac CT over recent years.

BROAD CLASSIFICATION OF ML

ML is an aggregate term which collectively encompasses a wide variety of analytical algorithms[11]. They can be simply divided into supervised learning, unsupervised learning, semi-supervised learning, deep learning and reinforcement learning[12,13] (Figure 1 and Table 1). Supervised learning requires labeled datasets or domains within the dataset to perform analytical actions[14]. Unsupervised learning does not require labels within a dataset and can analyze information in a very independent manner. For discussion purposes, it can be referred to as agnostic[2,15]. Hierarchical clustering, a type of unsupervised learning, can identify and distinguish new phenotypes within various cardiac diseases[2]. It has gained significant traction recently. Semi-supervised learning is a hybrid approach that utilizes properties present within supervised and unsupervised learning[16]. Reinforcement learning uses definitive reward conditions for the ML architecture to perform certain functions. Nevertheless, frequently not used in the field of cardiology[7]. Multiple studies have been documented to show the potential of ML in CT and CTA (Table 2).

Among all the available ML algorithms, deep learning is considered to have the most revolutionary potential[17]. In various sectors of commerce and industry, deep learning is being heavily utilized to unravel information within large troves of data[18]. From voice recognition software in Siri or Alexa to self-driving cars in google, deep learning is garnering significant interest[12]. The architecture of deep learning algorithms is similar to the arrangement of a human neuron[19,20]. It is structured in a series of layers, there is significant communication between the preceding and subsequent layers. It processes information in multiple layers and is more independent

Table 1 Type of machine learning

Types of machine learning	Function	Examples
Supervised learning (55)	Contains labels and outcomes, deduces inferences for prediction purpose	Includes logistic regression, ridge regression, elastic net regression, Bayesian and artificial neural networks
Unsupervised learning (55)	No labels, independently detects significant relationships.	Includes hierarchical clustering, k- means clustering, principal component analysis
Semi-supervised learning (55)	Properties of both supervised and unsupervised learning	Utilized in image and speech recognition
Re-enforcement learning (55)	Utilizes reward function to execute tasks	Utilized in medical imaging, analytics, and prescription selection

Table 2 Machine learning studies in computed tomography

Ref.	ML approach	Brief study description
ML derived CAC assessment		
Al'Aref <i>et al</i> [24]	Multiple ML algorithm	To use CAC and clinical factors for CAD prediction
Tesche <i>et al</i> [26]	ML algorithm	To compare ML derived CT FFR and CAC in CT
Kay <i>et al</i> [27]	ML algorithm	To identify phenotypes of left ventricular hypertrophy in combination with CAC
ML derived CT FFR assessment		
Zhou <i>et al</i> [31]	Multiple ML algorithms	To employ CT FFR for myocardial bridge formation prediction
Tang <i>et al</i> [32]	ML algorithm	To compare ML CT FFR, CTA and invasive angiography
Coenen <i>et al</i> [33]	Supervised learning	To identify CAD
ML derived evaluation of plaque characteristics		
Dey <i>et al</i> [34]	ML algorithm	To generate ML derived scores from plaque characteristics
Hell <i>et al</i> [35]	ML algorithm	To predict cardiac death from plaque characteristics from CTA
ML derived evaluation of epicardial adipose tissue		
Rodrigues <i>et al</i> [38]	ML algorithm	To segment and distinguish between different varieties of EAT
Commandeur <i>et al</i> [39]	Deep learning	To quantify EAT in CT
Otaki <i>et al</i> [40]	Supervised learning	To assess the relationship between EAT in CT and MFR in PET
Miscellaneous applications of ML in CT		
Baskaran <i>et al</i> [41]	Deep learning	To assess automatic and manual assessment of left and right cardiac structure and function
Al'Aref <i>et al</i> [42]	Supervised learning	To identify culprit coronary lesions in CT
Beecy <i>et al</i> [43]	Deep learning	To detect acute ischemic stroke in CT
Oikonomou <i>et al</i> [44]	Supervised learning	To utilize perivascular fat for cardiac risk prediction
Eisenberg <i>et al</i> [45]	Deep learning	To evaluate epicardial tissue for MACE events

CT: Computed tomography; CTA: Computed tomography angiography; CAC: Coronary artery calcium; ML: Machine learning; CAD: Coronary artery disease; FFR: Fractional flow reserve; EAT: Epicardial adipose tissue.

compared to other ML algorithms. As the complexity and size of the dataset increase, the performance of the algorithm improves significantly[21,22].

AUGMENTED CORONARY CALCIUM ASSESSMENT

Coronary artery calcium (CAC) measurement is heralded as a fundamental metric in coronary CT because it serves as a pivotal predictor of mortality and cardiac complica-

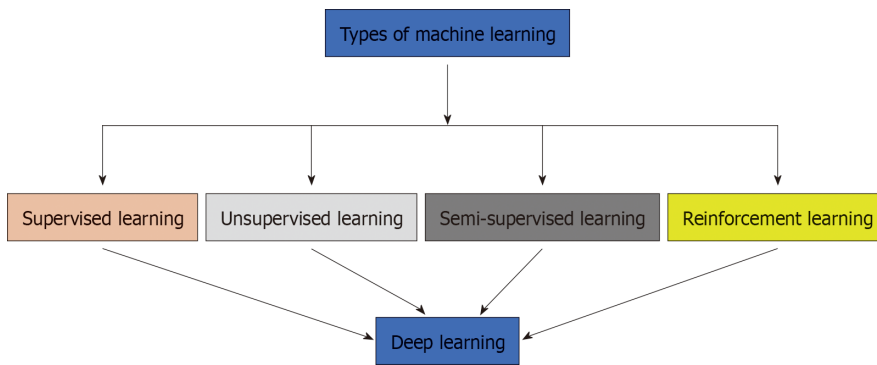


Figure 1 Brief overview of the progression of machine learning.

ations[23]. The Agatston scoring method is the conventional approach utilized to quantify CAC in coronary CT[19]. Furthermore, the CAC plays a diagnostic role in medical management, the CAC scores can be used to stratify patients and monitor medical therapy. However, CAC measurement can be quite tedious due to underlying artifacts, image noise, an abundance of calcifications, interobserver variability, and other factors[24]. The application of ML can significantly elevate the potential of CAC in CT.

Al'Aref *et al*[24] applied an ML architecture incorporating clinical factors in the CONFIRM registry with CAC for calculating the probability of CAD with CTA in a total of 35821 patients. It clearly showcased excellent AUC for ML and (CAC) (0.881) to other conventional approaches in their study [ML independently (0.773), updated Diamond- Forrester Score (0.682) coronary calcium (0.886)]. Hou *et al*[25] assessed the role of supervised ML to evaluate pretest likelihood of CAD in CTA with 6274 individuals. Their ML algorithm demonstrated superior discriminative capacity for CAD occlusion in comparison to traditional scoring metrics such as Modified Diamond Forester scores and CAD consortium score ($P < 0.001$). Tesche *et al*[26] exhibited superior performance of ML derived CT fractional flow reserve (FFR) in comparison to CTA with CAC, substantial distinctions in capability were noted and with propionate increases in Agatston scores ($P < 0.001$). Kay *et al*[27] integrated various algorithmic frameworks with radiomics for identifying new phenotypic characteristics regarding left ventricular hypertrophy (LVH) severity in CT with (CAC) assessment. As a result, ML frameworks are found to be efficacious in identification of LVH.

APPLICATION OF MACHINE LEARNING FOR CT FRACTIONAL FLOW RESERVE

Although CTA enables visual evaluation of a stenotic lesion, it lags behind invasive FFR for assessing the hemodynamic significance of coronary stenosis[28]. Coronary fractional flow reserve (CT-FFR) has become a suitable non-invasive modality for evaluating ischemic heart disease and chest pain[29]. Furthermore, it can perform this task without the requirement of additional medications or imaging. It provides functional and anatomic evaluation, this approach is steadily gaining momentum in CT imaging[30]. ML algorithms can calculate FFR in the absence of computational fluid dynamics and yield additional prognostic information[3]. It can substantially expand the arena of CT-FFR in CT imaging.

Zhou *et al*[31] evaluated CT fractional flow reserve (CT FFR) for estimating myocardial bridge formation by integrating several algorithms. Interestingly, the framework chose properties which contained superior AUC (0.75 ± 0.04) in comparison to clinical attributes (0.53 ± 0.09 , $P < 0.0001$), or CT- FFR prosperities (0.62 ± 0.06 , $P = 0.0127$). Tang *et al*[32] demonstrated that CT FFR with computational fluid dynamics was superior CTA and invasive angiography for detecting vessel-specific ischemia. This was particularly seen in intermediate lesions ($P < 0.001$ for all). Coenen *et al*[33] demonstrated excellent correlation between ML based CT FFR and deep learning in CAD ($r = 0.997$).

PLAQUE CHARACTERIZATION AND SEGMENTATION IN CAD

ML algorithms can provide additional insight regarding plaque characteristics in CAD and augment our understanding[2]. Dey *et al*[34] utilized a logitboost algorithm to produce an ML-derived risk score from plaque characteristics in CTA for 254 patients. The ML algorithm displayed a higher AUC (0.84) than individual CTA parameters including stenosis (0.76), total plaque volume (0.74), and low likelihood of CAD ($P < 0.0006$) (0.63). Hell *et al*[35] investigated the role of ML algorithms to predict cardiac death from coronary CTA through the utilization of plaque features in 2748 patients. The non-calcified plaque $> 146 \text{ mm}^3$ ($P = 0.027$), low density non-calcified plaque ($P = 0.025$), total plaque volume $> 179 \text{ mm}^3$, and CDD $> 35\%$ in any vessel were significantly associated with elevated risk of future cardiac death.

ML AUGMENTED EVALUATION OF EPICARDIAL AND THORACIC ADIPOSE TISSUE

Cardiac CT is deemed as the gold standard for evaluation of epicardial adipose tissue (EAT) quantification and assessment. EAT is a layer of adipose surrounding the heart and the accompanying coronary arteries. In addition, EAT is significantly linked with various cardiovascular risk factors, atherosclerosis of the coronary arteries, and CAD [36,37]. The application of ML algorithms can automate the quantification of EAT and greatly reduce the time of manual measurements. This can translate into greater clinical implementation in coronary CT.

Rodrigues *et al*[38] applied ML algorithms for segmenting and differentiating types of fat in CT. The ML platform was able to achieve 98.4% mean accuracy and a DICE similarity index of 96.8%. Commandeur *et al*[39] utilized a deep learning algorithm for quantifying EAT in coronary CT. Strong agreement was observed between automatic and expert manual quantification with a mean DICE score coefficient of 0.823 and an excellent correlation of 0.923 with EAT volume. Otaki *et al*[40] utilized a boost ensemble machine learning algorithm for assessing the association of epicardial fat volume from myocardial flow reserve (MFR) in non-contrast CT in positive emission tomography (PET). The ML composite risk score substantially increased risk reclassification of impaired MFR to EAT volume or coronary calcium score (IDI = 0.19 and $P = 0.007$, IDI = 0.22 and $P = 0.002$).

MISCELLANEOUS APPLICATIONS OF ML

In CT, ML has been applied in a variety of different situations with overwhelmingly positive results. Baskaran *et al*[41] assessed deep learning for assessing cardiovascular structures for CTA in 166 patients. The ML architecture corroborated in parallel to manual annotation in CTA for left ventricular volume ($r = 0.98$), right ventricular volume ($r = 0.97$) ($P < 0.05$). Al'Aref *et al*[42] utilized ML in CTA to detect precursor culprit lesion from patients with CAD. It exhibited a superior AUC for discriminating lesions in comparison to other ML derived frameworks ($P < 0.01$). Beecy *et al*[43] on CT for detecting acute ischemic stroke events. Interestingly, their AUC was 0.91 for automatic detection of infarction and had a 93% accuracy with interpretation of experienced physicians. Oikonomou *et al*[44] examined the capability of the random forest ML architecture from the radiomic profile of CTA derived coronary perivascular adipose tissue (PVAT) for identifying cardiac risk. It exceeded traditional risk stratification metrics for MACE prediction ($P < 0.001$). Eisenberg used deep learning for MACE prediction with EAT and other characteristics. The EAT in CT predicted MACE effectively (HR, 1.35, $P < 0.01$), inversely with attenuation (0.83, $P = 0.01$)[45].

BIG DATA UTILIZATION FOR PREDICTION OF OUTCOMES IN CT

Big data has emerged as a valuable resource that provides significant depth and understanding and is instrumental to the growth of ML in clinical medicine (Table 3) [5]. Due to size and magnitude, many important characteristics are often unnoticed by conventional approaches[6,46]. The implementation of AI with these immense expanses of data can yield additional information which can aid in medical management and clinical care.

Table 3 Big data utilization by machine learning in computed tomography

Ref.	ML approach	Number	Brief study description
Motwani <i>et al</i> [47]	Supervised Learning	10030	To predict 5-yr mortality from CT
Rosendaal <i>et al</i> [48]	Supervised Learning	8844	To predict major cardiac events from CT
Han <i>et al</i> [49]	ML algorithm	86155	To predict all-cause mortality from CT

CT: Computed tomography; ML: Machine learning.

Motwani *et al*[47] evaluated an ML framework to predict CAD in 10,030 patients for five-year mortality in comparison to traditional cardiac metrics in CT. Interestingly, the ML architecture exhibited a superior AUC (0.79) than CT severity scores (SSS = 0.64, SIS = 0.64, DI = 0.62) for five-year all-cause mortality prediction ($P < 0.0001$). Similarly, van Rosendaal *et al*[48] utilized an ML framework in CT with 8844 patients for detecting major cardiovascular events encompassing various attributes in relation to severity scores for CAD prediction. The ML derived AUC (0.771) was significantly higher in CT than conventional scoring parametric systems (0.685-0.701) for anticipating major cardiovascular events, with a notable difference ($P < 0.001$). Han *et al*[49] assessed an ML-derived predictive capacity for all-cause mortality in 86155 patients. Notably, the AUC (0.82) noted to be higher than Framingham risk score and other traditional metrics ($P < 0.05$).

EVOLVING BELIEFS AND FUTURE DIRECTIONS OF ML

It must be emphasized with great importance that cardiovascular disease is heterogeneous in nature[50]. It cannot be perceived as straightforward because disease mechanisms have intricate interactions among molecular, genetic, and environmental factors[22]. The process is very dynamic, it truly reflects the essence of ML algorithms. ML can integrate this information from multiple sources and analyze it in a variety of approaches. This can lead to the development of various genetic markers which can help guide medical management and monitor responses after therapy[6,51]. Furthermore, we can tailor treatment regimens appropriate to the genetic constitutional makeup of an individual, ML algorithms will facilitate the growth of precision medicine[12].

In current times, mobile devices, smartphone apps, and wearable devices are part and parcel of our daily lifestyles[52]. Telemedicine and ML algorithms are clearly intertwined in cardiovascular imaging and CT[1]. The information from these devices can be integrated with various parameters in cardiovascular imaging to yield additional insight regarding various cardiovascular diseases. In many underserved regions of the world, these devices can provide medical care and help direct patients towards appropriate intervention[1,53]. ML algorithms can analyze this information in real-time and help expedite this process[1]. These algorithms can serve as a bridge between different types of technology and cardiovascular imaging.

Although several algorithms have significant potential in computed tomography, deep learning has the most overwhelming potential[54]. It captures information through hierarchical levels of abstraction. As the computational prowess of graphical processing units (GPUs) continue to progressively evolve in conjunction with big data, the relevance of deep learning in computed tomography is becoming imminent. It is very effective in robust tasks such as image classification, image segmentation, and identification of various cardiovascular structures in CT, CTA, and cardiovascular imaging[20]. Furthermore, it does not require extensive training. The accuracy can be achieved by elevating the capability of the network or increasing the training set. This is a stark distinction in comparison to other ML algorithms[55]. Other algorithms entail a significant number of observations, computations, manual labor, and training to achieve optimal efficiency.

Randomized clinical trials (RCTs) are the gold standard in clinical research. The integration of ML algorithms could prove to be exceeding useful if implemented appropriately. Numerous RCTs fail to reach completion due to several factors which could include improper study design, inadequate number of participants, or lack of funding[56]. The integration of ML algorithms during the early or intermediate stage of an RCT could provide an outlook of different outcomes[5]. This information could

be used to restructure the RCT to obtain more successful outcomes. In addition, ML algorithms can enhance the randomization process in RCT[56].

LIMITATIONS OF ML

Though ML algorithms offer a significant promise for the future, it is far from straightforward. Several issues need to be resolved for successful implementation in clinical medicine. The potential of false discovery can occur with small databases, there is not enough information to properly train the algorithm[55]. Unfortunately, AI lacks a moral compass[57]. In addition, several unintentional biases can emerge during the process and could alter interpretation. The “black box” nature has always been an enigmatic property of ML algorithms, this has impeded its adoption in the medical field[2]. Investigators must have a proper research concept and plan before embarking on any ML-related task. As a result, engineers, physicians, and other members of a research team must play an active role in every stage of the ML algorithm[15,58]. Adjustments can be made to the algorithm to deliver clinically relevant information.

For any ML algorithm to thrive and grow, large information or databases is mandatory[15]. Obtaining this information can be complex and tedious. Data needs to be shared among institutions to allow training of the ML model[15]. This might require multiple IRB approvals. Information also needs to be de-identified before it can be shared. Many of these tasks can be time-consuming. Many types of imaging systems are frequently used for storing cardiovascular images. Nevertheless, each institution has their own unique protocols and there are differences in the acquisition process as well[2]. Some form of data standardization is required to facilitate data sharing and ML algorithm growth. If more information can be publicly available, it would be beneficial.

CONCLUSION

ML algorithms will have limitless potential in cardiovascular imaging, this has been evidenced in the field of CT. It will cause multiple paradigm shifts which will have a revolutionary impact in the field of medicine. These frameworks will automate several tasks, perform calculations, and aid as a supplementary tool for medical diagnosis and prognostication. By performing multiple tasks, physicians will have more time to spend with patients and be more focused on proper medical management. ML will serve as a long-lasting bridge between physicians and technology in clinical medicine.

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