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Artificial intelligence in coronary artery calcium measurement: Barriers and solutions for implementation into daily practice

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ABSTRACT

Coronary artery calcification (CAC) measurement is a valuable predictor of cardiovascular risk. However, its measurement can be time-consuming and complex, thus driving the desire for artificial intelligence (AI)-based approaches. The aim of this review is to explore the current status of CAC volume measurement using AI-based systems for the automated prediction of cardiovascular events. We also make proposals for the implementation of these systems into clinical practice. Research to date on applying AI to CAC scoring has shown the potential for automation and risk stratification, and, overall, efficacy and a high level of agreement with categorisation by trained clinicians have been demonstrated. However, research in this field has not been uniform or directed. One contributing factor may be a lack of integration and communication between computer scientists and cardiologists. Clinicians, institutions, and organisations should work together towards applying this technology to improve processes, preserve healthcare resources, and improve patient outcomes.

1. Introduction

Cardiovascular disease (CVD), including ischaemic heart disease and stroke, is the leading cause of death and disease burden worldwide, with over 500 million incident cases and 18 million deaths reported in 2019 [1]. An important indicator of CVD is increasing coronary artery calcification (CAC), which is concurrent with developing atherosclerosis to the point that its extent is predictive of cardiovascular events over time [2]. CAC is increasingly prevalent with age, more prominently in men [2–5]. CAC can be an asymptomatic condition without clinical manifestations, but CAC has been independently associated with CVD. This association is sufficiently strong that calculating a CAC score has been suggested to be a more accurate tool for cardiovascular risk stratification than the common Framingham risk score or other measures such as C-reactive protein level or carotid intima-media thickness [6]. Therefore, given its association with major cardiovascular events in asymptomatic individuals and its long-term nature (versus one-time variable measures such as blood pressure or cholesterol values, which can show differing results at different time points or under different circumstances), CAC volume measurement is currently used as a predictor of cardiovascular risk [6].

Coronary calcium quantification was first studied using electron beam computed tomography (CT), which was later supplanted by multidetector CT. A means of quantification of this coronary calcium volume was needed for standardised comparison and evaluation; thus, the Agatston score was developed. This score is calculated by summing lesions weighted by density and multiplied by a factor determined by maximum plaque attenuation [7,8]. Since its development, the Agatston score has been subsequently refined and supplemented by alternative measures, such as calcium volume score and relative calcium mass score [9].

Although CAC measurement is clinically useful, the effort required has driven the desire for the development of artificial intelligence (AI)-based CAC measurement tools. In busy clinical settings, time-consuming or complicated measurements are commonly omitted, sometimes to the detriment of patient care [10]. Additionally, coronary calcification is often heterogenous, meaning that scoring obtained from a specific vessel may underestimate the true risk of events, as calcification may be

Abbreviations: AI, artificial intelligence; BMI, body mass index; CAC, coronary artery calcification; CT, computed tomography; CNN, convolutional neural network; CNR, contrast-to-noise ratio; CVD, cardiovascular disease; DRL, diagnostic reference level; EAT, epicardial adipose tissue; FOV, field of view; MTF, modulation transfer function; PCCT, photon-counting CT; VNC, virtual non-contrast; VNI, virtual non-iodine.

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localised in a single vessel or plaque, or distributed throughout coronary vessels; location of calcium within the coronary arteries (e.g., proximal vs. distal) may have important effects on outcomes [8]. Some semi-automated methods for CAC quantification have begun to be developed and put into clinical use to address these issues, but they remain complicated [11,12]; in semi-automated CAC quantification by workstation (WS), WS identifies candidates for CAC. However, these candidates include pleural calcification, pericardial calcification, and calcification of the aortic/mitral valves. Users, usually radiological technologists but sometimes cardiologists or radiologists, must decide whether to adopt or reject each case themselves on a case-by-case basis. To reduce decision errors, training of these personnel is mandatory. Both this manual process and the required training are time-consuming, supporting the use of AI for CAC quantification.

Novel, AI-based tools for CAC scoring that can provide reliable measurement without additional effort from clinical staff or inconvenience for patients have the potential to overcome these obstacles [13]. The advantages of using AI to complete CAC classification tasks establish a rationale for its implementation. CAC score calculation requires time-consuming drawing of contours of identifying regions of interest by clinicians [14], and reliably replacing this labour with machine tasks would represent great savings in time, money, and human resources.

Generally, AI is defined as the use of computers to replicate human cognitive functions [15,16]. In healthcare settings, these functions include natural language processing to interpret unstructured data, such as clinical notes or patient statements, and machine learning to interpret structured data, such as medical images or genetic information. The nature of CAC measurements, which are based on medical images, means that this review will focus on the latter—machine learning. Current applications of AI in healthcare have largely focused on the interpretation of medical imaging; some successful examples of this include using AI to identify skin cancer subtypes, detect cerebral aneurysm and guide treatment decisions for cerebral infarction [15,17], and in the prediction of osteoporosis and fragility fractures [18–21]. Subsets and classifications of machine learning that are most notably being applied to CAC measurement include supervised learning, unsupervised learning, and deep learning (Fig. 1) [22].

Given these successes, it is clear that the future of CAC measurement and risk assessment will likely involve the integration of AI processes to some extent, dependent on their iterative refinement through research and the will of multidisciplinary teams of researchers and clinicians to adopt them. The aim of this article, therefore, is to review the current status of CAC volume measurement using AI-based systems for the automated prediction of cardiovascular events, and to make proposals for implementation of these systems into clinical practice to guide the detection and management of CVD.

2. Image acquisition and deep-learning algorithms

Currently, there exist several imaging modalities used to evaluate the heart. In clinical practice these include CT, magnetic resonance (MR) imaging, nuclear medicine (single photon emission CT, positron emission tomography), and ultrasound. Each of these has its drawbacks: MR and nuclear medicine are time-consuming for scanning and unsuitable for large-scale screening; ultrasound has the problem of interobserver reproducibility [8,10]. CT offers greater accessibility than other modalities and higher reproducibility than ultrasound.

Of notable applicability to CT, one particularly useful area of advancement in the AI field is the invention of artificial neural networks. These consist of many individual artificial 'neurons', emulating biological neurons in their reactions to specific inputs (that is, becoming activated or not, similar to the binary system of ones and zeroes used in computing) and modifying the connections between themselves via a training process [23]. This allows for increasingly accurate assessments and the ability to complete progressively complex tasks with greater speed.

In relation to clinical and radiological images, AI using these neural networks can be taught to classify images into defined categories if trained to identify specific pathological features on those images extracted by expert personnel [24], allowing classification into (for example) ranges of CAC scores (Fig. 2). The more extensive the training, the more precisely each of the characteristics can be weighted to predict outcomes with little prediction error.

Convolutional neural networks (CNNs) identify associations between complex input variables (in this case, medical images) and outcomes. They are made up of layers of nodes, each with an assigned threshold value; if the output of the node is above the threshold, the node is activated and sends the signal to the next layer of the network. CNNs are specifically applicable to medical imaging because of their ability to classify images into a preset category. With training, the network learns the best filters to apply to identify the image features that correspond to the specific categories [25].

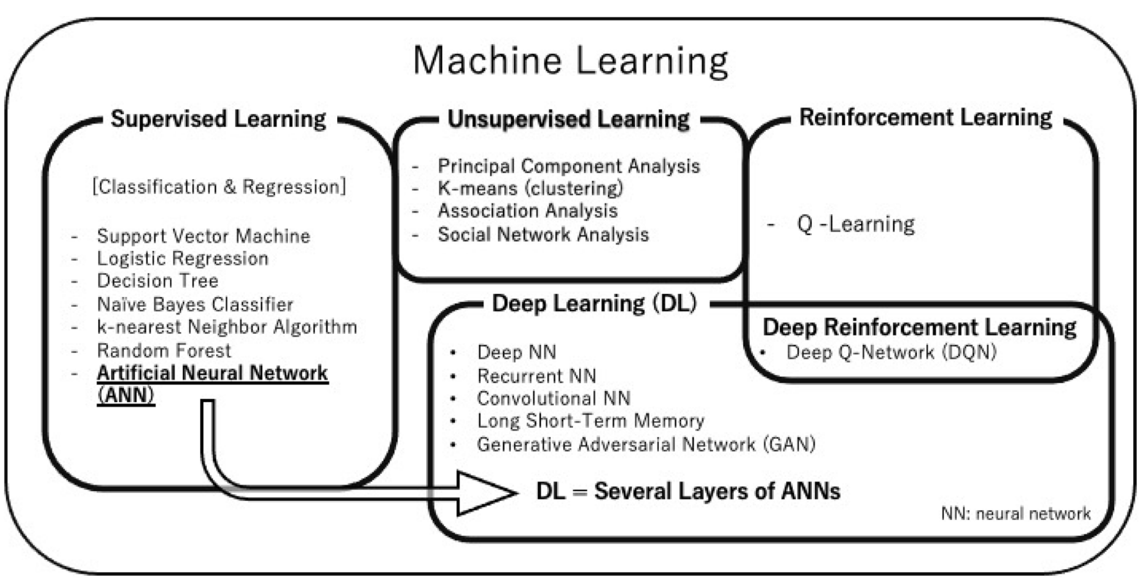

Fig. 1. A proposed classification of machine learning.

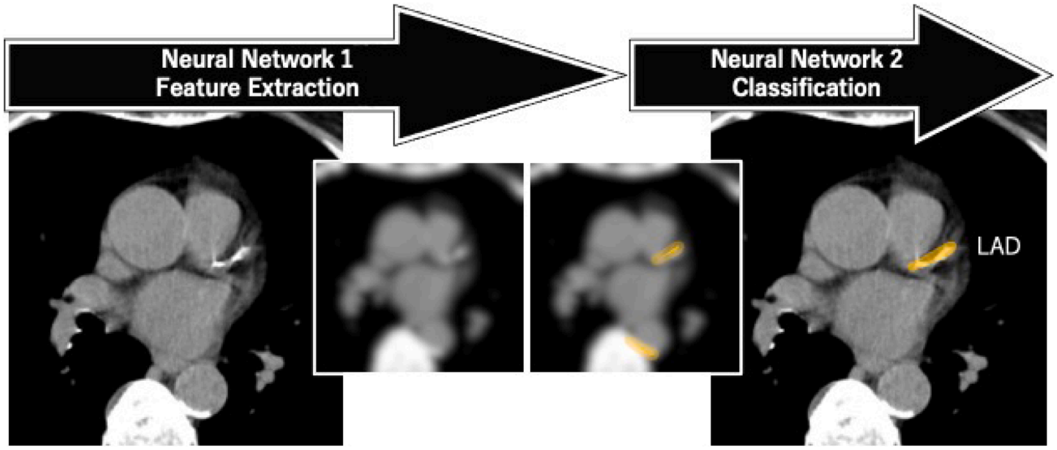

Fig. 2. Architecture of a deep-learning calcium scoring algorithm. This algorithm consists of two neural networks. The first CNN has a large FOV and detects candidate calcifications (voxels) on the image, labelling them on the basis of their anatomic location. The second CNN has a smaller FOV and detects true calcified voxels among candidates detected by the first CNN. Reproduced from "INNERVISION 38 (4) 2023" in Japanese with permission from Toshihide Yamaoka [93]. CNN, convolutional neural network; LAD, left anterior descending artery.

3. Current and ongoing research

The application of AI to medical imaging analysis has been a productive area of research in recent years. In 2018, an AI system that can diagnose diabetic retinopathy via images of the eye produced by a retinal camera became the first device that uses AI processes to be approved by the US Food & Drug Administration [26]. Multiple studies have used AI to analyse coronary CT imaging of various modalities for purposes other than CAC scoring, such as for classifying pericardial effusions [27]; these are well reviewed in Maragna et al. [10]. Some examples of these studies are in characterisation of epicardial adipose tissue (EAT) and pericoronary adipose tissue, where AI-powered solutions have been shown to correctly quantify EAT based on non-contrast cardiac CT [28,29].

A number of studies have applied AI specifically to CAC scoring [30–33]. One major goal of CAC scoring is to identify patients with stable coronary artery disease (CAD). The relationship between CAC and stable CAD is well established, notably that patients with a CAC score of zero rarely demonstrate obstructive CAD, showing better prognosis than their counterparts [34]; however, whether CAC quantification can reliably differentiate non-obstructive from obstructive CAD remains controversial [35]. Although evidence of a risk-reducing association with zero CAC in symptomatic patients is being accumulated, no large-scale studies have shown that it could be considered a gatekeeper across the range of pre-test probability of CAD [34].

An overview of the published studies to date is presented in Table 1. Notably, Lee et al. demonstrated high accuracy of AI in calculating CAC scores in a large sample using three CT cohorts and used AI to correctly assign cardiovascular risk stratification 93.9% of the time [36]. The use of a deep-learning method for calcium scoring has also been validated

Table 1
Application of artificial intelligence in automatic coronary calcium scoring.

Study	Patient group	Standard	Validation	ICC	Cohen's kappa	Accuracy
Wolterink et al., 2016 [82]	Patients with both CT angiography and calcium scoring CT (N = 250)	CSCT, CCTA	Internal	0.944	0.83	0.83
Cano-Espinosa, 2018 [32]	Non-ECG-gated chest CT scans (N = 1000)	Manually computed Agatston score	Internal	0.932	NR	0.76
De Vos et al., 2019 [38]	Cardiac CT (n = 903) and chest CT scans (N = 1687)	Manually computed Agatston score	External	0.98	0.95	0.99
Fischer et al., 2020 [14]	Coronary CT angiography (N = 194)	Manual calcium detection	External	N/A	0.85	0.903
Martin et al., 2020 [33]	Consecutive CT imaging patients (N = 511)	Manually scored CAC	External	0.985	NR	0.932
Van Velzen et al., 2020 [37]	Various nonenhanced CT from 6 datasets (N = 7240)	Semiautomatically labelled CAC and TAC	External	0.84–0.99	0.90	NR
Kamel et al., 2021 [30]	Patients who underwent cardiac CT and chest radiography within the same year (N = 1689)	Total and per-vessel Agatston scores	Internal	NR	NR	0.73
Lee et al., 2021 [36]	Previous cohorts of asymptomatic, symptomatic and valve disease in 4 CT models	Manually segmented CAC scoring	External	0.99	0.94	NR
Van Assen et al., 2021 [39]	Dedicated CAC CTs (N = 95) and chest CT only (N = 168)	Manually calculated Agatston score	External	0.921	0.74	0.7
Zeleznik et al., 2021 [44]	Cardiac-gated and non-gated CT from multiple asymptomatic and stable/acute chest pain cohorts (N = 5521)	Manual segmentations by expert CT readers	External	0.795	0.71	0.92
Watanabe et al., 2022 [40]	Dedicated CAC CTs (n = 315)	Calcification volume conventionally measured via workstation	External	0.81–0848	0.75–0.80	0.946
Xu et al., 2022 [31]	144 chest CT scans	CAC score manually measured on designated calcium scoring CT	External	0.90–0.94	0.72–0.82	NR

CAC, coronary artery calcium; CCTA, coronary computed tomography angiography; CSCT, cardiac calcium scoring computed tomography; CT, computed tomography; ICC, Intra-class correlation coefficient; κ, Cohen's linearly weighted kappa; NR, not reported; TAC, thoracic aorta calcification.

across a variety of CT protocols, showing good agreement with manual scoring [37].

CNNs were used in two separate studies to accurately identify calcifications in cardiac and chest CTs, extending automatic assessment of calcification scores to non-ECG-gated CT scans [38,39]. Watanabe et al. compared AI-obtained CAC volume scores versus commercially available workstations and Agatston score, with good correlation [40]. Fischer et al. used recurrent neural networks in a deep-learning algorithm to detect and quantify coronary artery calcium from coronary CT angiography in a cohort of patients with a wide range of calcification (including none); sensitivity, specificity, and diagnostic accuracy were generally good but were observed to be increased with better-quality data sets [14]. Furthermore, Dobrolińska et al. used CNNs to classify motion-contaminated images and assign CAC scores in four artificial plaques. Although these scores were not systematically compared with those of human observers, the results show the potential to avoid one of the limitations of machine-scored processes [41].

In related work, Commandeur et al. recently combined CAC score and EAT quantification into a machine-learning algorithm to predict outcomes such as myocardial infarction or cardiovascular death in an analysis of a large population (N = 1912) with a long duration of follow-up (14.5 ± 2 years). This algorithm proved to be more accurate in predicting these events than were either established clinical risk scores or CAC scores [42]. Another recent study showed that a comprehensive machine-learning model incorporating some 77 variables (including the CAC score, the number, volume, and density of CAC plaques, and extracoronary scores) was superior to ASCVD risk, CAC score, and a machine-learning model fitted using CT variables alone in the prediction of both CVD- and coronary heart disease-related death [43]. Zeleznik et al. found a deep learning-based calcium score to be strongly associated with cardiovascular risk in a retrospective study of patients from primary prevention cohorts (N = 20,084) across a broad spectrum of clinical scenarios [44]. These studies indicate how machine learning may allow the leveraging of all data within the CACS scan to improve risk prediction beyond the capabilities of the CACS itself.

Intriguingly, research has been carried out using scans conducted for other clinical purposes. For example, a study from the Netherlands was conducted using low-dose CT scans from trials of lung screening, demonstrating reliable cardiovascular risk assessment based on the lung cancer screening scans [45]; another study from the same institution applied deep-learning algorithms using a set of radiotherapy-planning scans from breast cancer patients [46]. The success of these efforts suggests that in some patients and situations, CAC scoring can be generated using scans undertaken for other reasons and applied to risk prediction for patients who have yet to develop any cardiovascular symptoms.

Of note, there are some notable differences in the accuracy reported by the various studies presented in Table 1. Possible reasons for this include differences in the competing AI technologies used or the training sets applied, or more prosaic reasons such as study design or patient cohorts; most likely these differences are related to the use of internal versus external validation cohorts, which are known to substantially affect the performance of machine-learning models [47]. Overall, however, the reported accuracy rates are generally high and can only be expected to improve with consistent application. A potential advantage is that there are several kinds of large cohorts that may be applied in AI analysis. This means that, if permitted, replication studies could be conducted with different AIs. Conversely, it should be noted that training data sets include some degree of uncertainty, which may introduce some skewness in specific cases; furthermore, when cohorts are analysed by different AIs as noted above, reproducibility is not guaranteed.

AI technology has been successfully used for automatic patient positioning [48] and image reconstruction (allowing for high-quality image reconstruction at fast speeds with low radiation doses) [49,50], as well as for CAC quantification. Still-newer proposed techniques employ three-dimensional encoder-decoder neural network architectures to generate CT-like volumes from single- and dual-view topograms [51]. Together, these techniques allow CT to be applied to CAC quantification to potentiate and simplify mass screening.

In addition to the potential of AI for direct CAC measurement, there exist further applications of algorithms for calcium scoring currently being explored, notably the possibility to create virtual non-contrast (VNC) non-iodine reconstruction from coronary CT angiography data. Dual-energy CT creates VNC images from contrast-enhancing scans using iodine-containing contrast agents; VNC images are calculated using a virtual non-iodine (VNI) reconstruction algorithm [52]. Several studies have shown the feasibility of CACS using VNC images, with generally good agreement with standard scoring techniques [53–55]. This approach could reduce the necessary dose of radiation by allowing the omission of native scans. Dual-energy CT can create mono-energetic images, as well; the use of these can reduce beam-hardening artefacts.

Photon-counting CT (PCCT) is an emerging technology in CT that may represent the next major milestone in that field [56,57]. Briefly, a PCCT system counts the exact number of incoming X-ray photons and measures their energy individually. Therefore, PCCT effectively filters out electronic noise, with resulting improvement in signal-to-noise ratio [58]. PCCT uses energy-resolving detectors, thereby enabling scanning at multiple energies, which can produce VNC images using a lower radiation dose than dual-energy CT. The images generated using PCCT additionally have higher spatial resolution than those produced by dual-energy CT, and studies to date show the possibility of superior performance using a VNI algorithm with PCCT [59] that may be improved upon further still by adjusting virtual mono-energetic image and iterative reconstructions [60–62].

Numerous studies have thus been conducted on different aspects of using AI to analyse CAC in a variety of settings, including the use of plain chest CT, low-dose CT for lung cancer screening, and source data of CT angiography. Re-evaluations of analytic algorithms and training datasets have also been conducted. These studies and their generally favourable results show the great potential of this emerging technology. However, most are isolated reports, and the emerging information lacks coherency and clearly defined applicability in the current clinical scenario of CAD. A specific gap in the evidence base is the lack of reproducibility when different AIs or methods are applied. To date, there is no established common ground for comparing the performance of separately trained AIs.

4. Implementation

Efficient implementation of these imaging biomarkers into clinical practice by the average practicing physician to guide detection and management of CVD will require planning and foresight. The proposals we present here provide a framework, although some aspects remain to be further clarified by ongoing or future research.

4.1. Training and optimisation

An important first step is the introduction of well-chosen training sets. A specific benchmark dataset for the heart already exists, but it consists of MR imaging and is not appropriate for CAC measurement [63]. Benchmark testing is mandatory for comparison of AIs. An example would be the LUNA16 (LUng Nodule Analysis) dataset for lung segmentation comprising 1186 lung nodules annotated in 888 CT scans) [64]. If appropriate datasets do not yet exist, scientific societies and medical professional associations should take the lead in establishing them [65].

Approaches to optimisation during training of the neural networks include Adam, optimiser and classical stochastic gradient descent. These are types of algorithms that help neural networks more accurately assign weights to specific inputs, resulting in faster and more accurate categorisation. Adam is an optimisation algorithm specially designed for deep neural networks that is being increasingly used; however, in some cases it is less effective than stochastic gradient descent.

4.2. Image requirements

For AI analysis, CT images must have a high contrast-to-noise ratio (CNR) and high spatial resolution. This must be balanced with the need to minimise radiation dose. New deep-learning image reconstruction techniques may assist in this, and they are already being used in routine CT scanning [66], although adaptation of dose levels and image reconstruction methods is mandatory [67,68].

However, van Velzen et al. demonstrated that AI methods adapted well to the addition of novel CT types in a single combined deep-learning model [37]. This may indicate that the type of image is not the most important characteristic, and that multiple types of CT imaging can be successfully processed.

4.3. Integration into other standard workflows

AI approaches may be applicable for CAC score assessment during chest CT for angiography [69] or for other reasons, such as lung-disease screening [31,70], eliminating the need for additional radiation exposure. Lung cancer screening, as recommended by the United States Preventive Services Task Force [71], may be an ideal opportunity for this, given the close associations among smoking, lung cancer, and CAD [72]. An example of this type of opportunistic screening was the recent NOTIFY-1 project, which used a validated deep-learning algorithm (with radiologist confirmation) to identify incidental CAC among patients with a prior non-gated chest CT. This led to more statin prescriptions and CAD testing in the patients randomised to notification of their primary care physician versus those randomised to continued usual care [73].

4.4. Patient selection

Certain patient characteristics may indicate obvious candidates for CAC screening using AI. The ACC/AHA Guidelines note that for patients with borderline or intermediate estimated 10-year risk of atherosclerotic cardiovascular disease, CAC assessment is a reasonable tool to reclassify that risk as higher or lower [74]. Adults with obesity may also be among candidates for CAC screening using AI, because of their higher risk of coronary atherosclerosis [75,76]. One combined approach could be to set a threshold incorporating the Brinkmann index (a measure of cigarette smoking) and the body mass index (obesity) [77] to identify patients well suited for analysis using AI. As noted above, however, the apparent ability to easily risk-stratify scans obtained during other processes, such as lung cancer screening, means that patients should not be excluded from AI analysis because they lack these characteristics or risk factors.

4.5. Implementation barriers and potential issues

In 2020, Bates et al. identified three impediments to rapid adoption of AI interventions, namely methodological issues in evaluating those interventions, lack of reporting standards for assessment of model performance, and issues at the institutional level [78]. External validation is a notable area that the authors found to be lacking in the development of most models; this will need to be resolved before models can be widely adopted. The future evaluation of AI models should also include external validation to avoid degradation of a model's performance when it is introduced into new areas. At the institutional level, the method of integrating AI is also important, whether it be for clinical decision support at the point of care, as part of a data-driven risk dashboard such as with laboratory results, or simply to flag patients for further evaluation or action.

Nevertheless, whatever approach or combination of approaches is used, it is important that any implementation plan does not automatically accept the results of AI analysis without scrutiny. Practical methods for human backup will need to be developed, including measures to flag patients for human review.

One issue that should be addressed is the so-called 'black-box problem', whereby it is unclear how an AI reaches a conclusion. Neural networks are very complex, and their individual steps are not necessarily understandable to people not trained in computer science. As a result, implementing AI may require a decision between an easily interpretable model that is less accurate versus a black box that is more accurate or efficient. A recent review by Petch et al. explores these issues in more detail and suggests a 'rule of thumb' framework around making decisions on when using black-box models may be appropriate [79]: in general, models should be developed using both interpretable and black-box methods, then assessed to determine if there is a difference in accuracy between the two. If not, the interpretable model should be used. If the black-box model is determined to be more accurate, the stakes of the decision should be considered; for lower-stakes decisions, a small improvement can justify the use of a black-box model, while for high-stakes decisions, the improved accuracy should translate to improved clinical outcomes of morbidity or mortality to justify its use.

There are also some potential privacy and ethical issues related to AI that need to be considered. As ever, the security of patient data must be paramount. Maintaining part of the dataset on cloud services could result in data security breaches, whereby data could be used to infer sensitive information and violate patient privacy. Additionally, the parameters of neural networks could reveal information on the training set when being used to train neural networks. Potential approaches to avoid these issues include integrating a differential privacy projection in the input layer or using encryption mechanisms when data are transferred. Yang et al. provide a useful overview of these considerations in the era of large biomedical datasets [80].

The characteristics of CAC scoring using AI suggest possible approaches in lower-resource or non-specialist settings, perhaps incorporating telemedicine or remote/centralised processing (Table 2). No major training of on-site staff is necessary, as the role of staff is limited to checking for appropriate segmentation of CAC and the validity of the results. A lack of resources, therefore, should not present an insurmountable barrier to implementation.

AI has the potential to predict cardiovascular risk precisely from several kinds of CT images, including non-ECG-gated chest CT, low-dose screening CT for lung cancer, and contrast-enhancing CT. Integration of AI into real-world practice will preserve clinical resources and improve patient outcomes. However, we cannot yet evaluate and compare aspects of the performance of several different AIs on common ground. Common benchmark datasets should be built, and guidelines for ideal training datasets should be produced by medical science societies to fill this important gap.

5. Future directions

As this field rapidly develops, further research is needed to address the gaps in the literature, both in terms of developing AI capabilities and applying them to the clinical setting. In this evolving field, new areas for exploration are emerging using a variety of different approaches before a critical mass of sufficient data accumulates in any specific area. Research protocols will therefore require standardisation to allow data from multiple studies to be amalgamated. Thus, it will be critical to build common datasets, similar to the LUNA16 lung cancer nodule analysis set aimed at CT detection of lung cancer locations and the reduction of false positives, to evaluate and compare AI approaches, including both ECG-gated and non-gated image sets of the same patients. It will also be important to determine requisites of image quality for AI analysis to assist in providing standardisation across fields.

Table 2
Recommendations for implementation of AI in CAC scoring.

Category	Recommendations
AI training	• Training sets should include large datasets that are representative of the full disease spectrum, include different scanning platforms, and well represent the population (sex, age and race) in which they are to be deployed • Validated with common, well-established benchmark datasets (if organised and available) • Training approaches should include integrated optimisation via Adam or stochastic gradient descent models
Workstream integration	• In daily clinical practice, candidate patients should be identified on quality assurance for images, with selected exams analysed with AI • In regular health check-ups that include CT, exams of people in higher risk groups (smokers, obese, or elderly persons) should automatically be analysed with AI
Technical recommendations	• An image reconstruction algorithm (kernel) should be chosen that has a combination of high CNR and high MTF • Artificial intelligence reconstruction should be used to reduce image noise and radiation exposure dose • Iterative reconstruction may be inappropriate • Photon-counting CT is preferable, if available, to reduce radiation dose
Staff training	• Doctors: AI results should be validated to determine whether segmentation of CAC is correct or not • Radiographers: To identify candidate patients in daily practice, training radiographers (staff for quality assurance of images) to recognise CAC is important
Patient identification in health check-ups or mass screening	• Smokers and ex-smokers with a high Brinkmann index • Obese patients with high BMI (over a threshold such as 30) [83] • Preoperative patients aged over a threshold such as 50 years [84] • Type 2 diabetes mellitus patients [85–88] • Haemodialysis patients [89] • Hyperuricemia [90–92] • Patients with coronary stent or implantation of arrhythmia device are not suitable for AI analysis, because of the risk of inappropriate segmentation
Errors and discrepancies	• AI results should include calculated results with annotated images indicating segmentation results for validation
Privacy and ethics	• If an AI system requires connection to an outside network service, the network should be sufficiently secured • Additionally, data that use an outside service must be anonymised

AI, artificial intelligence; BMI, body mass index; CAC, coronary artery calcium; CNR, Contrast-to-noise ratio; CT, computed tomography; MTF, modulation transfer function.

5.1. Identification and validation of image parameters

Modulation transfer function (MTF) is used in the evaluation of spatial resolution. Spatial resolution is usually substituted by voxel size, which is defined as the size of the field of view (FOV), the number of the matrix and slice thickness (0.5 mm to 10 mm). For example, at 320 mm of FOV, 512*512 of matrix and 3 mm thickness, the voxel size is calculated as 0.625 mm (320 mm /512 pixel) × 0.625 mm × 3 mm. The larger the voxel, the lower the sharpness (resolution) of the image. However, CT images are generated with several kernels (reconstruction algorithms); for example, the soft tissue algorithm is weighted based on contrast among anatomical structures, while bone kernel is weighted based on the borders between structures. Images of the identical voxel may therefore have different MTF.

Contrast-to-noise ratio indicates noise level; for example, the images of the bone kernel have more noise than those of the soft tissue kernel. The previous reports by van Assen and Watanabe discuss the same CNN AI (Siemens AI-Rad Companion Chest CT), but their studies obtained slightly different results [39,40]. This may be because differences in MTF and/or CNR affected the results of the analysis.

Similarly, establishment of diagnostic reference levels (DRL) is one of the steps in the overall process of optimisation. The International Atomic Energy Agency defines the DRL as a level used in medical imaging to indicate whether, in routine conditions, the dose to the patient or the amount of radiopharmaceuticals administered in a specified radiological procedure for medical imaging is unusually high or unusually low for that procedure [81]. DRLs, which are general guidelines for clinical operations and do not apply directly to individual patients and examinations, are practical tools to promote optimisation that were first successfully implemented in relation to conventional radiography in the 1980 s, and subsequently developed for other modalities in the 1990 s. Research is needed to establish DRLs for imaging that will be subjected to AI quantification and risk stratification of CAC scores.

5.2. Cooperation and other human factors

The widening scope of AI techniques has not fully resulted in their clinical implementation. To date, there has been limited cross-disciplinary work between computer science and the clinic, which persists as an important barrier to implementation. This may require a shift in mindset among clinicians and the gradual establishment of trust in complex systems that may appear inscrutable at first. It will be necessary to convince physicians and radiologists that implementing AI will aid them in their jobs rather than serve to replace them.

Given the lack of large-scale clinical testing to date, along with the limited validation of various AI software approaches, further research is required to address these gaps. However, as experience to date has shown, mere accumulation of volumes of disparate data is not sufficient to move the field forward; coordinated effort will be required to address the research gaps in an efficient manner. Researchers are strongly encouraged to report and publish their experiences in effectively integrating these processes into clinical practice, as well as when they encounter barriers that impede or prevent effective integration. Future research should focus on improving patient outcomes in various real-world situations. Additionally, for more effective use of AI, indications for AI analysis should be discussed and developed, and the profiles of patients suitable for AI analysis should be clarified.

6. Conclusions

The research to date on applying AI to CAC scoring shows the potential for automated scoring and CVD risk stratification. Overall, this body of research has shown its efficacy and a high level of agreement with categorisation by trained clinicians. However, as yet, the research in this field has not been uniform or directed. One factor that may have contributed to this is a lack of integration and communication between computer scientists and practicing cardiologists, and gaps in our understanding of the application of AI processes persist. Specifically, conducting large cohort studies will be necessary to realise the potential benefits of CAC measurement by AIs. Furthermore, the specific indications for use of AIs should be discussed, developed, and disseminated. Approaches to fill these gaps should include the establishment of guidelines for training datasets (including, for example, CT vendor, kernel, radiation dose, MTF, CNR, gating versus non-gating, male:female ratio, age) to avoid the potential for skewness. It will also be crucial to establish a common benchmark dataset (thereby establishing official external validation data) with which to compare AI performance.

The pace of new research in this field and its obvious utility and potential applications mean that integration of AI into cardiovascular imaging and risk stratification processes is likely a matter of time rather than a question of possibility. For this reason, we have proposed some general guidelines for implementation with which we hope to ensure its consistency, efficacy, and efficiency, leading to better management and improved long-term patient outcomes. We believe that clinicians, institutions, and organisations should work together toward applying this technology to improve processes, preserve healthcare resources, and improve patient outcomes in this disease, which has such a substantial global burden.

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