Use of Artificial Intelligence in Coronary Artery Calcium Scoring

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Abstract

Coronary artery calcium (CAC) scoring improves traditional risk-factor based coronary heart disease risk stratification. Here, contribution of coronary artery calcium scoring to traditional 10-year coronary heart diseases risk prediction scores and new artificial intelligence methods used to automate coronary artery calcium scoring were reviewed. Research shows that traditional risk factors tend to overestimate or underestimate the actual risk of coronary heart diseases, meaning that including CAC score to risk stratification has potential to reduce over- and undertreatment. The automated CAC scoring methods are shown to be accurate and significantly more time-effective than the commonly used semi-automated method.

Keywords: Coronary Artery Calcium Scoring; Artificial Intelligence; Traditional CAC Scoring; Coronary Heart Disease.

Introduction

Cardiovascular diseases (CVDs) are the leading causes of mortality and morbidity in the world, accounting for almost 18 million global deaths that represent 31% of all global deaths. Heart attack and stroke accounts for 85% of these deaths. Coronary atherosclerosis and resulting first episodes of potentially lethal or disabling myocardial infarction events often strike apparently healthy asymptomatic individuals. Therefore, there is a great interest in routine screening, early detection and primary prevention. Lifestyle modification and pharmacotherapy can lower the incidence of acute events in susceptible individuals. Statins are the main cholesterol-lowering drugs used for primary prevention of cardiovascular diseases. Traditionally, CHD risk is predicted by calculating the risk factor-based score, like Framingham Risk Score (FRS), that focuses on factors like age, sex, smoking, blood pressure, serum cholesterol level, and diabetes. However, there is growing evidence that including CAC in estimating CHD risk has a significant effect on treatment decisions. Therefore, the first part of the review evaluates the contribution of CAC scoring to traditional 10-year CHD risk prediction scores.

Coronary arteries are the vessels that supplies the oxygen-rich blood and nutrients to the heart. Anatomical changes such as narrowing of coronary arteries due to deposition of calcium and other substances like cholesterol obstruct supply of oxygenated blood and nutrients thus causing CHD. Fractional flow reserve (FFR) of a coronary artery in comparison to hypothetical 100% normal coronary artery tells about the functional / physiological status of a coronary artery after variable calcium and / or cholesterol deposits. A CAC score provides an estimate of the burden of coronary atherosclerosis; hence, it is used for CHD risk stratification. To obtain the score, a non-contrast gated cardiac CT scan is conducted, and areas with calcium are identified and quantified.
Figure 1: Computer tomography (CT) scan of the heart with and without presence of Calcification in Coronary Artery.²

Figure 1 shows the computer tomography (CT) of the chest with identified calcification which is used to calculate CAC score. The score produced may be an Agatston score (reflects the total area of calcium deposits along with the density of calcium), calcium volume score, or relative calcium mass score depending on the method.⁶ Commonly, CAC scoring requires manual identification of the areas that represent calcification however artificial intelligence enables clinicians to perform multiple tasks like processing on different atlases at the same time with more accuracy and least human error.

The second part of the review summarizes methods developed to automate CAC scoring with artificial intelligence.

**Contribution of CAC Scoring to Traditional 10-year CHD Risk Prediction Scores**

CAC has been studied since the 1980s, and several studies have shown that it is effective in estimating CHD risk and is accurate for risk stratification.⁷⁻¹² CAC scoring prevents overtreatment with lipid lowering drugs.¹³ Individuals with higher CAC score and low-risk factor score have higher mortality rate than those with low CAC score and high-risk factor score.¹¹,¹⁴

Multi-Ethnic Study of Atherosclerosis (MESA) risk scoring algorithm was developed to study prevalence of risk factors and progression of subclinical CVDs among multiethnic population. Inclusion of CAC with traditional risk factors in MESA score improves the risk prediction by up to 80%.¹⁰ Others,¹ compared MESA-CAC risk score with Reynolds Risk Score (RRS) and Atherosclerotic Cardiovascular Disease Risk Calculator (ASCVD). RRS overestimated the risk prediction for 30% of participants while ASCVD underestimated the risk for 23% suggesting that inclusion of CAC scores provides more accurate risk stratification.

**Use of AI to Automate CAC Scoring on Chest CTs**

Artificial Intelligence (AI) strives to develop mathematical models and algorithms that aim to mimic human intelligence to solve challenging problems. Artificial neural networks (ANN), inspired by the biological neural networks in human brains are one of the most influential technologies used to achieve this goal. Each artificial neuron can use its connections to receive and transmit signals to other neurons.

Neural networks have an input and an output layer which may have intermediate layers with connected neurons known as hidden layers. A neural network with multiple hidden layers is called a **deep neural network**. Whereas a **convolutional neural network** (CNN, or ConvNet) is a type of deep neural network, frequently used to process images from different domains.

Chest CT scans are often used for routine screening, for example in heavy smokers to detect lung cancer. With AI, information about the cardiovascular system, e.g., through CAC scoring, can easily be obtained at the same time. This is of importance as lung disease patients are also at a risk for cardiovascular diseases.¹⁵ Hence, several
methods have been developed to automate CAC scoring from chest CTs. The reviewed methods and their accuracy are summarized in Table 1.

**Table 1: Summary of automated CAC scoring methods and accuracy.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isgum et al. (2012)</td>
<td>Probabilistic coronary calcium map and statistical pattern recognition system</td>
<td>79% for CAC volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>82% for Agatston risk groups</td>
</tr>
<tr>
<td>Gonzales et al. (2016)</td>
<td>Connected component analysis</td>
<td>86% for Agatston scores</td>
</tr>
<tr>
<td>Cano-Espinosa et al. (2018)</td>
<td>convolutional neural network (CNN)</td>
<td>93% for Agatston scores</td>
</tr>
<tr>
<td>Sandstedt et al. (2019)</td>
<td>AI-based automatic post-processing software</td>
<td>93% for Agatston score, volume score, and mass score</td>
</tr>
<tr>
<td>De Vos, et al (2019)</td>
<td>3d image registration with CNN</td>
<td>93% for CAC</td>
</tr>
<tr>
<td>Fischer, et al (2020)</td>
<td>CNN with Long Short-Term Memory (LSTM)</td>
<td>90.3% for CAC</td>
</tr>
<tr>
<td>Lee et al. (2021)</td>
<td>Semantic segmentation with deep learning</td>
<td>93% for CAC</td>
</tr>
<tr>
<td>Gogin, et al (2021)</td>
<td>Ensemble of 5 CNNs with 3d UNet model</td>
<td>95.1% for CAC</td>
</tr>
</tbody>
</table>

In a study, a probabilistic coronary calcium map and statistical pattern recognition system to automate CAC scoring from chest CT scans. Location, texture, size, and shape features are used to represent coronary artery calcium lesions. Location features were determined by registering an input image to an atlas image and by extracting the location features from a map of a priori spatial probabilities of CAC. Chest CTs were registered to create a probability map. The detected CACs were used to obtain CAC volume scores and Agatston scores. Using 231 chest CT scans, the results showed 79% accuracy for CAC volume and 82% accuracy for classifying Agatston risk groups. The sensitivity of their method for CAC volume was 79.2% but only 58.6% sensitivity for Agatston risk groups.

Chest CT scans of 1500 patients were used to automate Agatston scoring. Firstly, bones were identified by connected component analysis so that they would not be misidentified as CACs. Secondly, machine learning-based object detector was used to detect the heart by finding the pulmonary artery and the aorta from the image. Thirdly, the region of interest was defined around the heart. After this, calcified voxels were identified and grouped in connected components to compute Agatston scores (Figure 2). The results showed 86% agreement with manual Agatston scores.
More recently, research has focused on the use of convolutional neural networks (CNN) which were trained to obtain Agatston scores directly from chest CT scans (Figure 3). Database of 5973 chest CT scans with Agatston scores was used, of which 4973 scans were used for training and 1000 scans for testing. The results showed that CNN was able to predict Agatston scores from the test set with 93% accuracy.

Figure 3: Regression Network Structure for CAC scoring. Three 3D convolutional layers with 3D max-pooling operations linearize the output. Dropout layers are used before the linearization operation and the output layers to prevent over fitting.

A study compared AI-based automatic post-processing software for automated CAC scoring and traditional semi-automatic CAC scoring that requires manual calcium identification. Three hundred and fifteen chest CT scans were used for both methods to determine Agatston score, the volume score, the mass score, and the number of calcified coronary lesions. The results showed that all outcomes between the automated and semi-automated method were in ~93% correlation. Additionally, the median time for the automated method was 9 seconds and 59 seconds for the semi-automated method. The study demonstrates that automatic CAC scoring is equally accurate to semi-automated scoring and significantly faster.

CAC has higher attenuation differences between lesions. To address this, Lee, et al has used coronary CT angiography (CCTA) to generate labeled data. This dataset is used with CAC images for pixel level classification. Finally, the image details are fed into a software (AVIEW CAC, Coreline Soft, Co. Ltd., South Korea) that determines the CAC score.
Figure 4: Labels from coronary CT angiography (CCTA) are transferred to CAC for registration purpose. These registered labels with CAC images are then forwarded to U-Net model (Adapted from Lee, et al 2021).

de Vos, et al\textsuperscript{19} proposed combination of two convolutional networks. One network is used for unsupervised atlas-registration and the second one is used for the calculation of calcium scoring (Figure 5). Atlas registration CNN is used for image registration to align all the input images in the same 3d space or field of view. This is done by fixing the atlas image and warp rest of the images available in dataset by finding the transformation parameters and by interpolation. Calcium Scoring CNN predict the calcium scoring from the image slices.

Figure 5: Image is first registered by Atlas registration Conv-Net to align the field of view which is then fed to calcium scoring Conv-net to find the CAC.\textsuperscript{19}

Fischer, et al\textsuperscript{20} proposed segmentation based deep learning method (CNN and LSTM) for calcified scoring but this was only 90.3% accurate. Gogin, et al\textsuperscript{22} proposed ensemble of 5 CNNs with 3d U-Net architecture. Each model is built with the depth of 4 levels having 16 initial filters. They used exponential linear unit as activation function. Residual connection is used in each Convolutional layer with batch normalization. Final decision about the classification is done by the majority voting for each voxel (3d pixel) by all the 5 CNNs and hence the CAC...
scoring is around 95% accurate. More recently, Zair et al. applied the preprocessing and extraction model prior to segmentation of 3D heart. The whole process as shown in Figure 6 estimates CAC score with an accuracy of 99%.

**Figure 6:** Pre-treatment phase - Image volume is passed through preprocessing step in which Region of interest (ROI) is extracted in the form of 3d bounding box. During binary classification for CAC segmentation, ROI is classified if it is CAC or not. If it is CAC classified, then in the next phase it is further classified into the specified class where it belongs.

**Conclusion**

Cardiovascular risk assessment can be improved using CAC scoring and artificial intelligence. CAC score enhances risk stratification with traditional risk factors and that CAC score on its own is effective in predicting CHD risk. Traditional risk factors tend to overestimate or underestimate the actual CHD risk, meaning that including CAC score to risk stratification has potential to reduce over- and undertreatment. Furthermore, several methods have been developed to automate CAC scoring. These methods are shown to be accurate and significantly more time effective as compared to non-AI based method that required a lot of human efforts, however more studies are required for cost and benefit analyses of automating CAC. Further research is recommended in investigating the effect of CAC score in reducing over- and undertreatment. Larger datasets are required for deep-learning system i.e., to evaluate the methods for coronary artery segmentation and calculation of CAC. Statistical parameters such as sensitivity, specificity, precision, recall and F1 score need to be defined and for this purpose several studies are required. Taken together, automated CAC scoring using deep-learning system coupled with electronic medical records can help the clinicians identify patients at high risk in time-efficient manner.

**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
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References


**Highlights**

- CHD risk stratification with traditional risk factors leads to over- and underestimations of the CHD risk
- Including CAC score to risk stratification provides more accurate results and has potential to reduce over- and undertreatment
- Artificial intelligence can be used to automate CAC scoring for more time-effective methods
- Future directions for research include quantifying the reduction in over- and undertreatment after including CAC score in risk stratification and cost-effectiveness of automated CAC scoring