Original Article

Predicting the Risk of Cardiovascular Diseases Based on Retinal Fundus Images Using a Deep Learning Model

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Abstract

Purpose: To develop a deep learning model to predict the risk of cardiovascular diseases (CVDs) events based on features found in fundus images.
Materials and Methods: We developed a predicting model for cardiovascular diseases based on retinal fundus images using the deep learning method. We trained our model using 2,091 retinal fundus images obtained from 211 patients. Our dataset included demographic information of each person, conventional CVD risk factors, CVD risk estimated number (calculated using the Framingham method), strokes and heart attack incidents during 5 years (patients who were referred to the ICU or CCU), and retinal fundus images for each person. We used receiver operating characteristic (ROC) analysis to assess the accuracy of our classification model.
Results: Our proposed algorithm was able to identify high-risk individuals from no-risk individuals with 83 % accuracy and a high confidence level (AUC = 0.91, P value < 0.0001). The results also showed that our model could predict cardiovascular events such as stroke with a probability of 72 % (AUC = 0.83, P value < 0.0001). In comparing our model's ability to predict CVD risk with the Framingham risk score, the Framingham model's accuracy was 65 % in our dataset (with a best AUC of 0.78).
Conclusion: Our deep learning prediction model developed based on retinal fundus image findings to predict the risk of CVD, showed a relatively high accuracy. Its accuracy was higher than traditional prediction models like the Framingham model and comparable to other models based on fundus images for predicting CVD.

Keywords: Prediction; Cardiovascular Diseases; Retina; Fundus Image; Deep Learning.

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Introduction

According to the report by the world health organization in 2021, cardiovascular diseases (CVDs) are the leading cause of death globally [1]. Approximately 17.9 million people die due to CVDs each year (32 % of all global deaths) [1]. More than 80 % of these deaths are due to heart attacks and strokes, and about 30 % of these deaths occur prematurely in people under 70 years of age [2]. CVD risk assessment is essential for identifying groups at risk and preventing the associated mortality [3].

The conventional methods for estimating the risk of CVDs, such as the Framingham Risk Score, QRISK, and Reynolds Risk Score, have not made the desired progress in predicting the occurrence of CVDs [4]. The main reasons for this poor performance might be methodological shortcomings, incomplete presentations, and lack of external validation [4]. Today, new problem-solving methods based on artificial intelligence and machine learning, along with the ability to store and process big data, such as medical images, have provided more accurate methods for predicting diseases [5]. Medical images provide data that require to complex processing methods and models [6]. Retinal fundus images contain important biomarkers, such as blood vessels, which allow the investigation of small vessels directly, non-invasively, quickly, and at low cost [7]. Studies have suggested that the state of retinal vessels indicates the state of cerebral, coronary, and peripheral vessels of the body [7-9]. Additionally, markers of cardiovascular disease or conventional risk factors, such as hypertensive retinopathy and cholesterol emboli, can often manifest in the eye [10].

Deep learning are neural networks in consisting of a large number of hidden processing layers, capable of performing complex representations of input data. These representations are often difficult or impossible for humans to understand. These networks can extract a series of non-linear features from the data that the human brain is unable to process and discover.

Based on these assumptions; we have developed a model to predict the risk of CVD events based on features of retinal fundus images. Our model is based on neural networks and deep learning concepts, which are related to machine learning.

Materials and Methods

We used a subset of second phase dataset of the “Shahroud Eye Cohort” study [11,12]. In total the information from 211 patients with a mean age of 55.6 ± 6.2 years was used in the present study. Shahroud University of Medical Sciences provided us with the dataset. This study was exempted from obtaining ethics committee approval due to nature of study using data previously obtained from the patients. Our dataset included demographic information of each person, conventional CVD risk factors, CVD risk estimated number (calculated using the Framingham method), strokes and heart attack incidents during 5 years (patients who were referred to the ICU or CCU), and retinal fundus images for each person. See table 1 for more details.

Model development

A deep neural network (DNN) is a mathematical model with the ability to learn, inspired by the human brain. A DNN is composed of multiple processing layers and can extract a series of features and relationships between them from input data, which the human brain is unable to process and discover. To achieve our aim (CVD risk prediction based on retinal fundus

Table 1: Information regarding data used to develop the prediction model

Number of participants:		211
Number of fundus images:		2091
Demographic factors	Age: mean ± SD	55.6 ± 6.2
	Gender: (% male)	44.7 %
Conventional risk factors	Total cholesterol: mean ± SD	193.7 ± 42.1
	HDL cholesterol: mean ± SD	40.32 ±11.02
	Triglyceride: mean ± SD	181.2 ± (99.6)
	Fasting blood sugar: mean ± SD	105.9 ± (44.5)
	Blood pressure disease: percent	59.7 %
	Diabetes: percent	21 %
	Smoker: percent	20 %
Framingham Risk Assessment: % of individuals at risk		28.4 %
Occurrence of stroke / heart attack: number of incidents reported		21

images), we used a convolutional neural network (CNN), a type of DNN that is suitable for solving classification problems with matrix-structured input data such as images.

Researchers often face data limitations in healthcare problems, so models are developed based on the "transfer learning" approach. In this approach, knowledge obtained in other scientific fields is used. In this study, we used the Inception-v3 model, which is trained with natural images from the ImageNet dataset. We retrained this model with our dataset based on the "fine-tuning" approach, which does not require retraining the lower layers that have extracted general features (such as corners and edges). Only the upper layers of the model were trained. There was no recommendation for the number of layers to be trained; so we determined them by trial and error.

The CNN models include many parameters in the training phase. The value of the parameters is determined according to the labels of the images in complex and repetitive training processes. At the end of each iteration, the prediction accuracy is calculated on the tuning data. After obtaining the parameters with acceptable prediction accuracy, the model will be general enough to predict the labels and can classify new images.

We divided our development dataset into three components: a 'training' dataset, a 'tuning' or 'validation' dataset, and a 'test' dataset (part of the data the model was not trained on). This segmentation was based on 'cross-validation' method.

One of the most important and common challenges in transfer learning is the issue of "overfitting". Overfitting occurs when the model is well-trained and shows high accuracy on the validation dataset but does not perform well on test data. This typically happens when the training dataset is relatively small and the developed model is relatively complex. In this study, we used "data augmentation" and "regularization" techniques to address the overfitting problem. We also employed early stopping criteria to help avoid overfitting. Early stopping terminates training when the model's performance on a 'tuning dataset' stops improving.

We used TensorFlow (available at http://tensorflow.org) and Keras (available at http://keras.io), open-source software libraries, to implement, train, and evaluate the model.

Evaluating the algorithm

We evaluated our classification model's performance using the area under the curve (AUC) metric. To evaluate classification models, there are standard evaluation criteria based on the "confusion matrix." AUC is the area under the receiver operating characteristic (ROC) curve, which plots the true positive rate against the false positive rate at different threshold values.

Results

We have developed an image processing model based on deep learning method for CVD risk prediction. We trained our model using 2,091 retinal fundus images obtained from 211 patients from the Shahroud Eye Cohort dataset.

Accuracy of the proposed model

Our proposed algorithm was able to identify high-risk individuals from no-risk individuals with 83 % accuracy and a high confidence level (AUC = 0.91, P value < 0.0001). The results also showed that our model could predict cardiovascular events such as stroke with a probability of 72 % (AUC = 0.83, P value < 0.0001). We used ROC analysis to assess the accuracy of our classification model. According to this analysis, we estimated 0.22 as the threshold point, meaning that if the estimated risk number is greater than 0.22, we classify the result as risky. The efficiency criterion, or the true positive rate, for our model was estimated at 100 %. In other words, our model was able to fully identify individuals who had experienced a stroke as positive. However, there were also cases where individuals who had not experienced a stroke were identified as positive by our model.

Comparison with the framingham model

In comparing our model's ability to predict CVD risk with the Framingham model using our data, our model achieved an accuracy of 83 % (AUC = 0.91, P value < 0.0001), which was better than the Framingham model's accuracy of 65 % (with a best AUC of 0.78).

Discussion

This study aimed to investigate the application of smart technologies in the health sector, focusing on predicting CVD using retinal fundus images. Predicting cardiovascular diseases and preventing acute incidents resulting from them, such as strokes, are of great importance [13]. Analyzing the challenges in this area reveals that conventional models used to predict the risk of these incidents in the clinical setting have failed to address this issue adequately [14].

We evaluated the proposed model in this study from several aspects: the algorithm's ability to classify high-risk individuals from non-risk individuals, the algorithm's ability to predict stroke and heart attack, a comparison of the algorithm's predictive power for stroke with the Framingham model, and finally, a comparison of the algorithm's predictive power for stroke with other deep learning algorithms in previous studies.

Our proposed algorithm was able to identify high-risk individuals from no-risk individuals with 83 % accuracy and a high confidence level (AUC = 0.91). The results showed that our model could also predict cardiovascular events such as stroke with a probability of 72 % (AUC = 0.83). When comparing our model with the Framingham model's results in predicting the occurrence of stroke and heart attack, our proposed model, with an accuracy of 72 % (AUC = 0.83), was able to better predict the occurrence cardiovascular events such as stroke compared to the Framingham model, which had an accuracy of 65 % (with a maximum AUC of 78 %).

In comparison with other studies on predicting cardiovascular events using deep learning-based retinal fundus image processing, our proposed model reported a better AUC than the baseline study by Poplin et al., [10] (AUC = 0.83 in our study versus 0.7 in their study). Another study by Lee et al., [15] which used a multimodal model including clinical risk factors and fundus photographs, achieved an AUC of between 0.78 and 0.87 when using two different databases, which is in line with our findings.

In conducting this research we encountered some limitations that can be addressed in future studies. Although the quality of images and the accuracy of variable measurements in the Shahroud Eye Cohort dataset were sufficiently high, our main limitation was the "imbalance" in the data. Imbalance in fundus images is primarily due to two factors: imbalance in foreground and background pixels and imbalance in the number of samples across different classes. Foreground-background imbalance, which occurs in many works related to fundus images, refers to the small number of pixels in the feature under study, such as lesions or blood vessels, compared to the much larger number of pixels in the corresponding background [16]. Future studies can reduce the impact of this imbalance by using detection networks to extract the region of interest before feeding the images into the algorithms.

Another suggestion for future research is to help generalize the model's results. Most models in the field of medical image processing face the challenge of generalizability due to fundamental differences between images resulting from differences in imaging equipment, as images are captured by different cameras with varying settings, resolutions, and lighting intensities. This issue, known as "domain shift" is one of the challenging topics in generalizing deep learning models [17]. To reduce the effect of domain shift, domain adaptation methods can be used [18].

Conclusion

Our deep learning prediction model developed based on fundus image findings to predict the risk of CVD, showed a high accuracy. Its accuracy was higher than traditional prediction models like the Framingham model and comparable to other models based on fundus images for predicting CVD.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.