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Evaluate the Correlation Between Electrocardiogram Age and Cardiovascular Disease Using a 12-lead ECG Dataset

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Abstract. Leveraging deep learning and vast clinical datasets can reveal crucial, previously indiscernible patterns in electrocardiogram (ECG) records, enhancing the diagnosis and assessment of cardiovascular diseases. In this study, we first construct a large-scale clinical 12-lead ECG dataset, then exploit the potential of deep learning models to analyze ECG data and identify a significant link between a patient's cardiovascular health and the discrepancy between their chronological (CHR) age and the age as predicted from ECG data. Through analyzing ECG records, the research determines correlations between predicted ECG age and CHR age in different populations. The results demonstrate ECG age is strongly correlated with CHR age only in the normal population, while the correlation is weaker in the cardiovascular disease population. Further analysis showed that when the ECG age is higher than the CHR age, the individual has a higher risk (the average is 1.64 times higher) of developing various types of cardiovascular disease. Conversely, if the ECG age is lower, they tend to have a lower risk (the average is 0.72 times lower). This evidence suggests that the difference between the ECG age and the CHR age can be viewed as a marker for cardiovascular health.

Keywords. Electrocardiogram, Age prediction, Deep learning, Cardiovascular disease

1. Introduction

Electrocardiogram is the most commonly used non-invasive test for assessing cardiovascular disease (CVD). Cardiologists can infer whether a patient has a specific disease by analyzing feature points and waveforms in the ECG[1]. Although this

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method is time-consuming and laborious, with the recent development of end-to-end models, efficient diagnosis of electrocardiograms with deep learning models has achieved great success [2-3]. However, ECG signals may often hide subtle signals and patterns that do not conform to traditional knowledge and are not recognizable to the naked eye [4]. Therefore, it is meaningful to use deep learning, along with large-scale clinical datasets, to explore information that is not intuitively reflected on the ECG and to analyze some features or knowledge not yet discovered by humans.

It is known that neural networks can predict a person's age based on an ECG [5-6]. We assessed whether the discrepancy between the ECG age and the CHR age could represent the cardiovascular health status and be related to cardiovascular disease. We collected ECG test records from hospital emergency room visits over four years, retaining only one ECG record per patient to avoid "cross-contamination". We trained a model based on a one-dimensional convolutional neural network with 12-lead ECG signals as input and the patient's actual age as a label. The correlation between ECG age and CHR age in different populations was then evaluated in unseen ECG recordings, and the difference between the two was used as a marker of cardiovascular health. The groups with differences greater than 8 or less than -8 were used as experimental groups, and the group with differences between -8 to 8 as the control group. The relationship between the different types and heart disease was evaluated using relative risk and odds ratio.

The experimental results show that among the normal population, there is a high correlation between the predicted age and actual age, while among the CVD population, the correlation between the predicted age and actual age is low. The risk of developing myocardial infarction, atrial fibrillation, and atrial flutter is 1.18, 1.37, 2.07, 1.64, and 1.92 times higher, respectively, for individuals whose predicted age is 8 years older than their actual age than those with comparable predicted and actual ages. Conversely, individuals whose predicted age is 8 years younger than their actual age have respectively 0.96, 0.67, 0.61, 0.55, and 0.82 times the risk of developing ST-T changes, conduction block, myocardial infarction, atrial fibrillation, and atrial flutter than those with comparable predicted and actual ages. The conclusion is that the risk of developing cardiovascular disease is higher when the ECG age is higher than the CHR age, and lower when the ECG age is lower than the CHR age. There is a significant correlation between the difference in ECG age and CHR age, and cardiovascular disease.

2. Methods

2.1. Data Sources and Study Population

We collected records of 12-lead electrocardiogram tests conducted at Shanghai First People's Hospital, affiliated with Shanghai Jiao Tong University, from January 2018 to March 2021, totaling 162,622 records. The ECG sampling rate was 500 Hz, with lengths ranging from 500 to 133,500. As shown in Fig. 1, we first excluded patients under 16 years old and over 90 years old and retained only one electrocardiogram record for patients with multiple cardiac examination records to avoid "cross-contamination" when dividing datasets. Furthermore, we also discarded records with significant interference and invalid test results. Based on this, we divided the data into training and test sets at a ratio of 7:3. From the training set, we selected 10,000 records for model verification, and the remaining records were used for model training. In the test set, we filtered out electrocardiogram records diagnosed by doctors as normal(NORM), ST-T change(ST_T), atrial fibrillation(AF), conduction block(CD), myocardial infarction(MI), and atrial flutter(AFL) for further analysis.

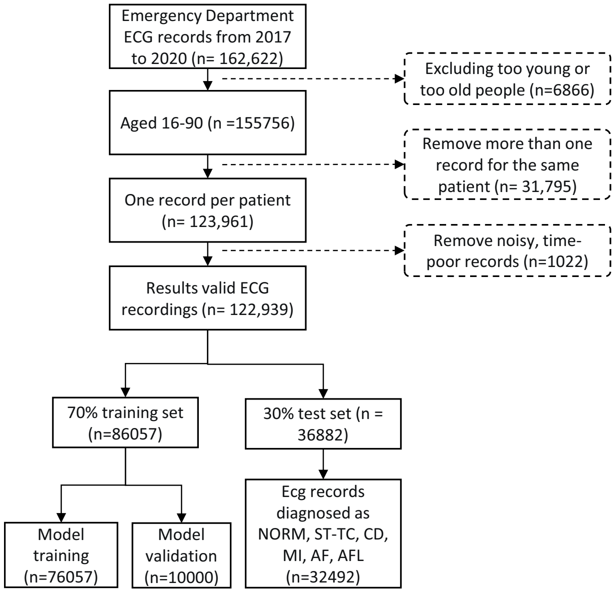

Figure 1. Clinical dataset inclusion and exclusion criteria.

2.2. Overview of Algorithm

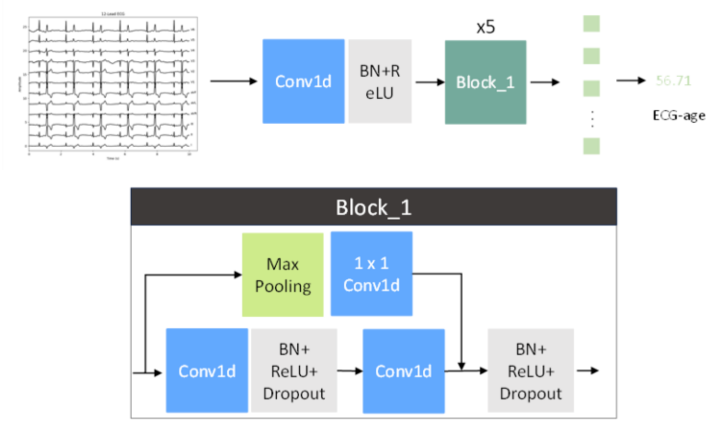

Figure 2. ECG age predicted convolution neural network architecture.

We implemented a one-dimensional Resnet using the Pytorch framework [7]. For electrocardiogram samples in the training set, those shorter than 4096 are padded with zeros on both ends, and those longer than 4096 are truncated to get a fixed-length electrocardiogram signal, which is then fed into the model. The model's output is the predicted age for the record. As shown in Fig. 2, the model c comprises an initial convolutional layer succeeded by five sets of residual structures, each embodying two convolution layers. After each convolution layer, batch normalization is applied to rescale the output and then goes through the Rectified Linear Unit (ReLU) as an activation mechanism, with Dropout applied after that. The convolution kernel size is 17, with the five residual blocks having 64, 128, 196, 256, and 320 respectively, and the feature numbers are 4096, 1024, 256, 64, and 16 respectively. In the residual connections[7], max pooling and convolution with a kernel size of 1 are added to make the size match the signal in the main branch. Our approach makes use of the Adam [7] optimizer, which is applied with an initial learning rate set to 0.001, aiming at the minimization of the weighted mean squared error. During training, if the loss of the validation set does not improve over seven consecutive epochs, the learning rate is reduced by a factor of 10. With a total span of 50 epochs for the training, we opt for the model that exhibits the most superlative performance on our validation set throughout the optimization. This chosen model is then deployed as our final one.

2.3. Models Evaluation and Statistical Methods

For the ECG records in the test set, we use the model to obtain their ECG age, then evaluate the correlation between ECG age and CHR age in different populations using the mean square error (MSE) and Pearson correlation coefficient(PCC), thereby indirectly assessing the accuracy of the model's predicted ECG age compared to the actual age. We assume that the disparity between the predicted ECG age and the chronologic age may serve as a biomarker for a cardiac condition, we will classify the disparity between the predicted ECG age and chronologic age into three categories: greater than 8, less than -8, and between -8 and 8. We used relative risk (RR) [8] and odds ratio(OR)[9] to assess the relationship between this cardiac status marker and cardio-related diseases. RR refers to the risk of disease occurrence in an exposed group relative to a non-exposed group in an experiment, calculated as RR= (incidence rate of the exposed group/incidence rate of the non-exposed group). OR refers to the chance of disease occurrence in the exposed group relative to the non-exposed group in an experiment, calculated as OR= (exposed number/non-exposed number in case group)/(exposed number/non-exposed number in the control group). In this study, the exposed groups refer to the two groups with age differences greater than 8 and less than -8, and the non-exposed group is the one with an age difference between -8 and 8.

3. Results

3.1. Age Estimation

Since the ECG age predicted convolution neural network's output is a continuous variable, we compute the statistics of the absolute error, as well as the population correlation. Fig. 3 illustrates a scatter plot of the ECG age vs. CHR age in various populations. For the test dataset, the average absolute error in the normal population is 7.99±10.34 years, with a PCC of 0.80; in the population with ST-T changes, the average absolute error is 8.60±11.03 years, with a PCC of 0.76; in the population with conduction blockages, the average absolute error is 8.57±10.85 years, with a PCC of 0.66; in the population with myocardial infarctions, the average absolute error is 9.74±11.16 years, with a PCC of 0.62; in the population with atrial fibrillation, the average absolute error is 8.76±10.94 years, with a PCC of 0.38; in the population with atrial flutter, the average absolute error is 9.89±11.94 years, with a PCC of 0.38, as shown in Table 1. This suggests that although the model is trained uniformly across all populations when ECG age in different populations, the correlation and error between the predicted age and the CHR age are smaller in the normal population, but the ECG age and the CHR age of the population with CVD have a lower correlation and a larger error.

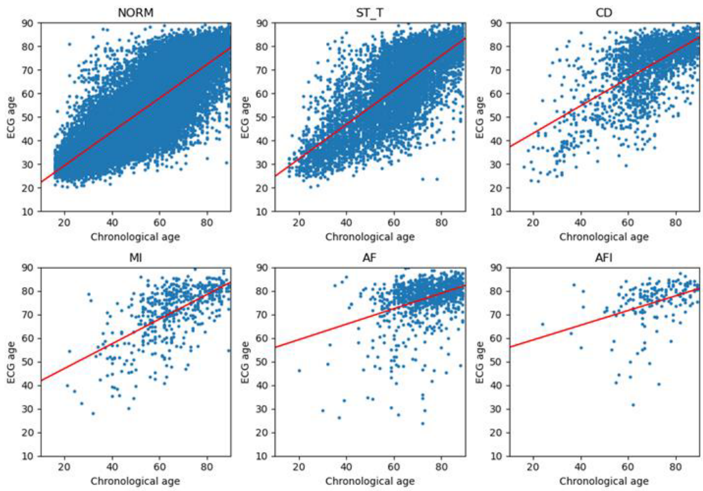

Figure 3. ECG age vs. CHR age in different populations. The red line is the correlation fitting line.

3.2. Diff-age as a Cardiovascular Marker

Table 1. MAE, PCC, RR, OR values of ECG age and CHR age among different populations

Population	**MAE**	**PCC**	**RR of ECG-Age Exceeds CHR Age by >8**	**RR of ECG-Age Less Than CHR Age by 8**	**OR of ECG-Age Exceeds CHR Age by >8**	**OR of ECG-Age Less Than CHR Age by 8**
NORM	7.99±10.34	0.8	0.93	0.99	0.72	0.97
ST_T	8.60±11.03	0.76	1.18	0.96	1.24	0.95
CD	8.57±10.85	0.66	1.37	0.67	1.4	0.66
MI	9.74±11.16	0.62	2.07	0.61	2.1	0.61
AF	8.76±10.94	0.38	1.64	0.55	1.67	0.55
AFL	9.89±11.94	0.38	1.92	0.82	1.92	0.83

Based on the analysis above, we assume that there is a correlation between the difference in ECG age and CHR age, and CVD. As shown in Tab. 1, the risk of diseases such as ST-T changes, conduction block, myocardial infarction, atrial fibrillation, atrial flutter, etc., in those whose predicted age is 8 years older than their actual age, is respectively 1.18, 1.37, 2.07, 1.64, and 1.92 times as high as that of those whose predicted age is equivalent to their actual age. While for those whose predicted age is 8 years less than their actual age, the risk of such diseases is respectively 0.96, 0.67, 0.61, 0.55, and 0.82 times of those of equivalent predicted and actual age group.

In addition, in several groups of people with cardiovascular diseases, the OR values for the group whose predicted age is 8 years greater than their actual age are all greater than 1, indicating a positive correlation, while the OR values are all less than 1 for groups of people whose predicted age is less than their actual age by 8 years, which shows a negative correlation. From this, we can reasonably speculate that the older the ECG age compared to actual age, the greater the risk of cardiovascular disease. Conversely, the younger the ECG age compared to the actual age, the smaller the risk of cardiovascular disease.

4. Conclusion

In summary, we explored the correlation between the difference in electrocardiogram age and actual age with several cardiovascular diseases. First, we built a real clinical dataset with ECG as the input and the actual age as the predicted value to train a deep learning model and then used this model to predict the ECG age on unseen ECGs. There is a strong correlation between the predicted age and the actual age in the normal population, but there is a smaller correlation and larger error in the population with cardiovascular diseases. The risk of cardiovascular diseases is higher in the population where the predicted age is 8 years older than the actual age and lower in the population where the predicted age is 8 years younger than the actual age.

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