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Research article

Prediction and verification of the effect of psoriasis on coronary heart disease based on artificial neural network

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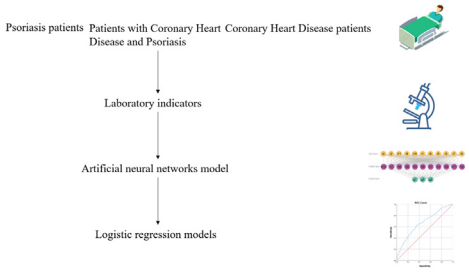
GRAPHICAL ABSTRACT



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ABSTRACT

Background and objectives: Psoriasis is an independent risk factor for coronary heart disease. It is important for predicting the complications of coronary heart disease in patients with psoriasis.
Methods: In this study, related cases were collected from the case system of Qingdao University, and commonly used laboratory indicators were extracted. Artificial neural network (ANN) and logistics regression analysis were used to learn to distinguish psoriasis patients, coronary heart disease patients, and psoriasis patients with coronary heart disease. We identified independent risk factors for coronary heart disease in psoriasis patients that exacerbate coronary heart disease symptoms in patients with psoriasis.
Findings: Analysis shows that the accuracy of the ANN model was higher than 79%. It was determined that age, chlorinated, phosphorus, magnesium, low-density lipoprotein, triglycerides, high density lipoprotein and total cholesterol are independent risk factors for coronary heart disease in patients with psoriasis. Similarly, gender, age, chlorinated, magnesium, triglycerides, and high density lipoprotein are risk factors that exacerbate coronary heart disease symptoms in patients with psoriasis.
Interpretation: The presented approach is a valuable tool for identifying psoriasis patients, coronary heart disease patients, and psoriasis patients with coronary heart disease. It can also serve as a support tool clinicians in the diagnostic process, by providing an outstanding support in the diagnostics prevention of coronary heart disease in psoriasis.

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1. Introduction

Psoriasis is a common, chronic, recurrent, inflammation- and immune-mediated skin disease that usually presents with varying degrees of skin itching and sharply demarcated erythematous plaques with whitish scales (Boehncke and Schön, 2015). A systematic review of worldwide epidemiology of psoriasis showed that the prevalence of psoriasis ranged from 0.51% to 11.43% in adults and 0%–1.37% in children (Michalek et al., 2017). Owing to the breadth of research on psoriasis, an increasing number of studies have found that psoriasis has gone beyond the scope of simple skin diseases to a multi-system chronic inflammatory disease accompanied by multiple related coexisting diseases, such as metabolic syndrome (Gisondi et al., 2018), malignant tumor (Chiesa Fuxench et al., 2016), chronic kidney disease (Wan et al., 2013), non-alcoholic fatty liver disease (Maybury et al., 2019), and atherosclerotic vascular disease (Kimball et al., 2010; Xu and Zhang, 2012). Among them, atherosclerotic disease is significantly affected by psoriasis; moreover, psoriasis is an independent risk factors for coronary heart disease (CHD) (Hadi et al., 2021).

CHD is a coronary vascular disorders that manifests primarily as atherosclerosis caused by epicardial coronary artery obstruction, which leads to insufficient blood supply to the myocardium. Related studies have postulated that the inflammatory and immune cells may play an important role in the process of the CHD (Harrington et al., 2017) because the inflammation blood biomarkers are elevated in patients with psoriasis and CHD (Boehncke, 2018). The systemic inflammation caused by psoriasis may lead to insulin resistance, which in turn leads to endothelial cell dysfunction and, eventually, atherosclerosis (Boehncke et al., 2011). In the immune system, Cytokines (e.g., interferon-α, interferon-γ, IL-1β, IL-6, and TNF-α) are excessively secreted in psoriasis and can effectively promote the activation of T cells and macrophages (Alalaiwe et al., 2021; de Alcantara et al., 2021). The activated T cells and macrophages have been shown to enhance the process of atherosclerosis (Gisterå and Hansson, 2017). In recent years, some researchers have observed that psoriasis patients may have a higher risk of CHD than normal people (Siegel et al., 2013); this has been confirmed by Białecka in a cross-sectional study (Białecka et al., 2021). In summary, psoriasis was considered to be an independent risk factor that can enhance the formation and progress of coronary atherosclerosis via multiple pathway and mechanisms.

It is therefore important to provide evidence that psoriasis can promote the formation and progression of coronary atherosclerosis. In the past decade, owing to the ongoing breakthrough and rapid development of deep learning in the medical field, new methods have become available for medical research (Choi et al., 2020). Artificial neural network (ANN) is a deep learning model construction method currently used to solve data mining and classification problems in multiple fields with good results (Yang and Wang, 2020). In this study, we employed the ANN method to construct two- and three-class models based on multiple laboratory indicators. The two-class model provides clinical evidence for psoriasis in aggravating CHD and provides predictors for coronary atherosclerosis in psoriasis. The three-class model demonstrates the effectiveness of ANN in distinguishing the CHD group, psoriasis group, and CHD + psoriasis group through laboratory indicators.

2. Method

2.1. Cases collection

The data of 4360 patients, who were treated at the Affiliated Hospital of Qingdao University from 2016 to 2021, were collected for this study. The patients were divided into three groups: CHD group, CHD + psoriasis group and psoriasis group. The inclusion criteria for the psoriasis group were patients diagnosed with psoriasis without any cardiovascular disorders, thyroid related disorder, and malignancies. The inclusion criteria for the CHD group were patients diagnosed with CHD without psoriasis and any other cardiovascular disorders, thyroid related disorder, and malignancies. The inclusion criteria for the CHD + psoriasis group were patients diagnosed with psoriasis and CHD without any other cardiovascular disorders, thyroid related disorder, and malignancies. From these clinical cases, 11 commonly used laboratory indicators (six routine cardiovascular related indexes and five trace element related indexes, Table 1) were extracted as input indicators. The input indicators were preprocessed to ensure that all indicators were quantified and avoided vacancies before being used for model training. This study was approved by the Affiliated Hospital of Qingdao University Review Board (QYFY WZLL 26701).

2.2. Model construction

The ANN model was constructed using the Python 3.6 (https://www.python.org/). The multilayer perceptron (MLP) model consists of three layers: input layer, hidden layer, and output layer. The MLP ANN used predictive factors consisting of input and output layers (group division) to define the complex relationship between inputs and outputs (Figure 1).

The patients in our study cohort were also completely randomly allocated; 80% of the total sample is used as the training set, the remaining 20% is used as the test set, and then, 30% of the training set is randomly selected as the validation set. They were used for the establishment of ANN models. Once the MLPANN was trained, it was then used to estimate the results from new input data.

To better understand the impact of psoriasis on CHD, we constructed one three-classification model and three two-classification models separately based on the three groups.

2.3. Model settings

In this study, the StandardScaler class from the sklearn function was used for data standardization. The sigmoid function was used as the activation function of the input and hidden layers, and the softmax function was used as the activation function of the output layer. The RMSProp was the optimizer for this model construction and the loss function was set as categorical cross entropy. The learning rate was 0.1, the rho was 0.9, the epsilon was 0, the decay was 0, the training period was 200, and the model training was completed when the training period reached 200. In addition to this, we chose Support Vector Machine (SVM) as a comparison to understand the application value of ANN in this field. In order to avoid the accuracy of the model being too high or too low, each model was run 10 times, and the average of the 10 runs was taken.

Table 1. Database parameters with identifiers.

Id	Parameter
I0	Gender
I1	Age (years)
I2	Lactate dehydrogenase
I3	Low-density lipoprotein
I4	Triglycerides
I5	Creatinine
I6	High density lipoprotein
I7	Total cholesterol
I8	Chlorinated
I9	Phosphorus
I10	Sodium
I11	Potassium
I12	Magnesium

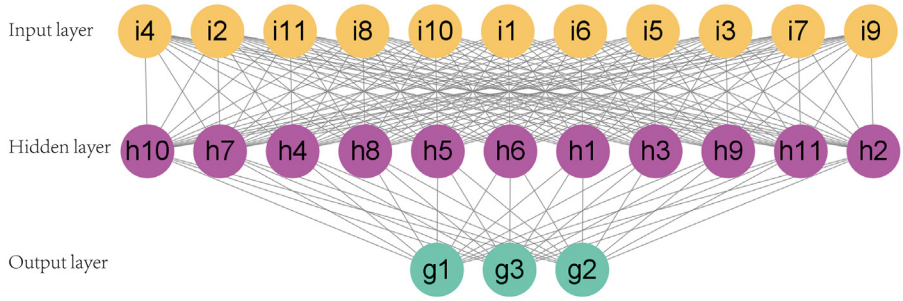

Figure 1. Schematic illustration of multilayer perceptron.

Table 2. Distribution of gender and age factors by class.

parameter	value	individuals	CHD	CHD + PSO	PSO
Gender	Male (1)	1511	1190	104	217
	Female (0)	1342	1181	48	113
age	<60	673	403	37	233
	≥60–80≤	1726	1542	94	90
	>80	454	426	21	7

2.4. Independent risk factor assessment

We constructed binary logistic regression models (CHD group and CHD + psoriasis group, CHD + psoriasis group and psoriasis group) to identify the main independent risk factors for psoriasis, causing and exacerbating CHD using the SPSS Statistics 25 software (SPSS IBM Corporation, Armonk, NY, USA). An adjusted odds ratio (OR) with 95% confidence intervals (CI) was used, and a p value <0.05 was considered statistically significant.

2.5. Statistical analysis

The Graphpad Prism 9 software (GraphPad Software Inc., La Jolla, USA) was used to perform statistical analyses. Normally distributed continuous variables are expressed as mean ± standard deviation, while non-normally distributed continuous variable are expressed as interquartile range. The characteristics of the participants among No CHD group, CHD + psoriasis group, psoriasis group were compared using Chi-square tests, or Kruskal-Wallis test. Statistical analysis: $p < 0.05$ was considered statistically significant.

Table 4. Accuracy of model.

Groups	ANN Loss	ANN Accuracy	SVM
CHD group, psoriasis group	0.242 ± 0.003	0.914 ± 0.002	0.906 ± 0
CHD group, CHD + psoriasis group	0.222 ± 0.003	0.937 ± 0.001	0.941 ± 0
Psoriasis group, CHD + psoriasis group	0.482 ± 0.005	0.773 ± 0.008	0.68 ± 0
CHD group, psoriasis group, CHD + PSO group	0.427 ± 0.003	0.870 ± 0.001	0.856 ± 0

Each value is expressed as mean ± standard deviation.

3. Result

3.1. Features of patients

According to the inclusion and exclusion criteria, a total of 4360 patients were considered for model training, including 723 psoriasis group, 3330 CHD group, and 307 CHD + psoriasis group. After preprocessing, a total of 2854 patients were considered for model training, including 330 in the psoriasis group, 2371 in the CHD group and 152 in the CHD + psoriasis group (Table 2). Table 3 is the analysis of each laboratory indicators in each group (Table 3).

3.2. The accuracies of the three-classification model, two-classification model and SVM model

We separately constructed a three-classification model and three two-classification models, and the results showed that ANN can effectively

Table 3. Analysis of disaggregating data according to the parameters and groups.

Parameter	CHD (N = 2371)	CHD + psoriasis (N = 152)	Psoriasis (N = 330)	Value P
Age	70(64, 77)	69(60, 75)	48(33, 61)	<0.0001
Chlorinated	105.1(103, 107)	104.925(102, 107)	105.85(104, 107.275)	0.0013
Phosphorus	1.09(0.97, 1.21)	1.07(0.92, 1.18)	1.16(1.02, 1.3075)	<0.0001
Sodium	142(140, 143.1)	142(140, 143.125)	141.3(139.5, 142.8)	0.0004
Potassium	4.1(3.86,4.34)	4.115(3.875, 4.3125)	4.095(3.89, 4.3)	0.9701
Magnesium	0.93(0.88,1)	0.93(0.8578, 0.98)	0.9(0.8325, 0.96)	<0.0001
Lactate dehydrogenase	171(148, 197.5)	173.5(148, 196.3175)	164(139.475, 192.325)	0.0128
Low-density lipoprotein	2.67(2.06, 3.33)	2.57(2, 3.0925)	2.335(1.9025, 2.8575)	<0.0001
Triglycerides	1.17(0.85, 1.64)	1.395(0.9725, 1.9925)	0.965(0.68, 1.44)	<0.0001
Creatinine	77(63.5, 88.1)	74.8(58, 93)	82.1(71.85, 92.425)	<0.0001
High density lipoprotein	1.3(1.1, 1.53)	1.21(1.04, 1.41)	1.095(0.94, 1.3075)	<0.0001
Total cholesterol	4.61(3.81,5.465)	4.37(3.65, 5.2425)	3.98(3.3625, 4.7475)	<0.0001

Kruskal-Wallis H test or Chi-square test. Normally distributed variables are expressed as mean ± standard deviation, non-normal variables are expressed as median (IQR) and categorical variables are expressed as percentage (%).

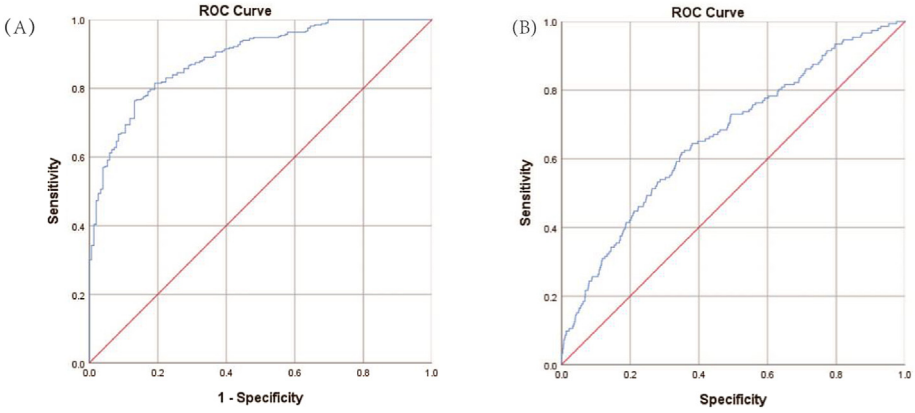

Figure 2. ROC curves. ROC curve of psoriasis group and psoriasis + CHD group, area = 0.889, p < 0.01, 95% CI = 0.86–0.918 (A). ROC curve of CHD group and psoriasis + CHD group, area = 0.665, p < 0.01, 95% CI = 0.617–0.71 (B).

Table 5. Binary logistic regression model for CHD group and CHD + psoriasis group.

Parameter	B	OR	95% CI	P
Gender	-0.776	0.465	0.327–0.661	p < 0.01
Age	-0.021	0.98	0.965–0.994	P = 0.007
Chlorinated	-0.048	0.954	0.914–0.994	P = 0.026
Phosphorus	-0.613	0.542	0.23–1.276	P = 0.161
Sodium	-0.02	0.981	0.93–1.034	P = 0.468
Potassium	-0.051	0.95	0.641–1.409	P = 0.8
Magnesium	-0.1888	0.151	0.028–0.821	P = 0.029
Lactate dehydrogenase	0.001	1.001	0.999–1.002	P = 0.475
Low-density lipoprotein	-0.097	0.907	0.758–1.087	P = 0.29
Triglycerides	0.206	1.229	1.106–1.367	p < 0.01
Creatinine	0.001	1.001	0.999–1.003	P = 0.204
High density lipoprotein	-0.808	0.446	0.272–0.731	P = 0.001
Total cholesterol	-0.092	0.912	0.796–1.045	P = 0.183

Table 6. Binary logistic regression model for psoriasis group and CHD + psoriasis group.

Parameter	B	OR	95% CI	P
Gender	-0.121	0.886	0.588–1.336	P = 0.565
Age	-0.09	0.914	0.897–0.931	p < 0.01
Chlorinated	0.103	1.109	1.046–1.175	p < 0.01
Phosphorus	2.198	9.008	3.529–22.993	p < 0.01
Sodium	-0.025	0.976	0.909–1.048	P = 0.496
Potassium	0.006	1.003	0.573–1.756	P = 0.991
Magnesium	-1.769	0.171	0.026–1.13	P = 0.067
Lactate dehydrogenase	-0.001	0.999	0.997–1.001	P = 0.455
Low-density lipoprotein	-0.387	0.679	0.532–0.867	P = 0.002
Triglycerides	-0.808	0.446	0.34–0.585	p < 0.01
Creatinine	0	1	0.998–1.001	P = 0.365
High density lipoprotein	-0.991	0.371	0.201–0.685	P = 0.002
Total cholesterol	-0.438	0.645	0.531–0.784	p < 0.01

identify CHD group, psoriasis group and CHD + psoriasis group based on the 11 common laboratory indicators (accuracy = 0.87). The results of the three two-classification model showed that ANN can effectively distinguish between the CHD group and psoriasis group (accuracy = 0.91), CHD group and CHD + psoriasis group (accuracy = 0.94), and psoriasis group and CHD + psoriasis group (accuracy = 0.77). The results of the SVM model show that the SVM also can distinguish the CHD group and the psoriasis group (accuracy rate = 0.91), the CHD group and the CHD + psoriasis group (accuracy rate = 0.94), the psoriasis group and the CHD + psoriasis group (Accuracy = 0.68), the three-classification (accuracy = 0.86) (Table 4). This proves that ANN can distinguish psoriasis patients, CHD patients, and patients with psoriasis and CHD through conventional cardiovascular-related and trace element-related indicators.

3.3. Independent risk factor assessment

In this section, first, we build a binary regression analysis model based on 11 laboratory indicators. We found that the binary regression analysis model can effectively distinguish between patients with CHD and patients with CHD and psoriasis (area = 0.889, p < 0.01, 95% CI = 0.86–0.918), and can effectively distinguish between patients with psoriasis and patients with CHD and psoriasis (area = 0.665, p < 0.01, 95% CI = 0.617–0.71) (Figure 2). Then, we present the construction of two binary logistic regression model based on each laboratory indicator for the assessment which laboratory indicators is the main independent risk factors for psoriasis causing and exacerbating CHD. As listed in Table 5, in the CHD and CHD + psoriasis groups, the main independent risk factors were gender, age, chlorinated, magnesium, triglycerides, and high density lipoprotein (Table 5). We initially thought these laboratory indicators are independent risk factors for psoriasis-exacerbating CHD. In Table 6, in the psoriasis group and CHD + psoriasis group, the main independent risk factors were age, chlorinated, phosphorus, magnesium, low-density lipoprotein, triglycerides, high density lipoprotein, and total cholesterol (Table 6). We initially assumed these laboratory indicators are independent risk factors for psoriasis-causing CHD. In summary, we believe that age, triglycerides, and high-density lipoprotein are independent risk factors that cause and exacerbate CHD in patients with psoriasis.

4. Discussion

In the last decade, the awareness of psoriasis has shifted from an inflammation and immune-media cutaneous disorder to a systemic inflammatory and immune-media disorder (Kamiya et al., 2019). The clinical study of Piaserico S, Ellis CN, and Lerman JB found that patients with psoriasis have larger epicardial adipose tissues and higher risk of coronary microvascular dysfunction, noncalcified coronary plaque burden, and high-risk plaque prevalence, which is aggravated by the progression of the psoriasis (Piaserico et al., 2019; Ellis et al., 2021; Lerman et al., 2017). Coronary atherosclerosis represent atherosclerosis of psoriasis complication, which have become a focus of systemic treatment for psoriasis (Osto et al., 2012; Torres et al., 2013). At the protein level, although there are not many relevant studies, it is currently known that IL6, PCSK9, IL17A, TNFα, and IL12 mediate the progression of coronary atherosclerosis in patients with psoriasis; however, its detailed mechanism of action remains unclear

(Wang et al., 2016; Garshick et al., 2021; Cao et al., 2021; Wegner et al., 2021; Ikonomidis et al., 2017). Therefore, it is essential to predict the occurrence of CHD in advance for the prevention and treatment of psoriasis patients with coronary atherosclerosis complications.

In this study, we constructed a disease model for psoriasis combined with CHD based on the laboratory indicators to offer a method that can effectively distinguish between the CHD patients, psoriasis patients, and patients with CHD and psoriasis. To the best of our knowledge this is the first such study using ANN methods. We separately constructed a three-classification model and three two-classification models, and the accuracy of the four models was higher than 0.79, with the highest accuracy being 0.93. The three-classification model proves that ANN can effectively distinguish the three groups. The two-classification models prove that ANN model can effectively recognize psoriasis patients who may have CHD early by learning laboratory indicators, and provide clinicians with relevant evidence to prevent the occurrence of CHD. These evidences prove the application prospects of ANN in patients with psoriasis and CHD. However, the accuracy of the CHD group and the psoriasis + CHD group was low. We initially considered that psoriasis only promoted the occurrence and development of CHD, and did not have an additional impact on the condition of CHD.

Next, we constructed binary logistic regression models and found that binary regression analysis can also be used to distinguish psoriasis patients with CHD and psoriasis, CHD patients, and CHD and psoriasis patients. The result showed that gender, age, chlorinated, magnesium, triglycerides, and high density lipoprotein are independent risk factors that exacerbate CHD in patients with psoriasis. Age, chlorinated, phosphorus, magnesium, low-density lipoprotein, triglycerides, high density lipoprotein and total cholesterol are independent risk factors that cause CHD in patients with psoriasis. Among them, age, triglycerides, and high-density lipoprotein are both independent risk factors that cause and aggravate CHD in patients with psoriasis.

ANN is a valuable tool that can be used to identify patients with psoriasis, coronary heart disease, and psoriasis patients with coronary heart disease. It provides an excellent support decision-making tool for the diagnosis of coronary heart disease complications in psoriasis patients. It also supports clinicians in the treatment of coronary heart disease complications of patients with psoriasis, especially in building models based on routine clinical laboratory indicators, which can alleviate economic burdens to patients. In addition, we also found independent risk factors that may cause psoriasis in patients or exacerbate coronary heart disease—this provides more clinical support as decision-making tools. Apart from that, we choosed SVM to compare with ANN. The results show that the accuracy of ANN is higher than that of SVM in most situations, especially in the psoriasis group and CHD + psoriasis group, which also reflects the superiority of ANN in this filed. However, in order to be closer to clinical application, the indicators selected in this study are biased towards routine laboratory examinations rather than coronary heart disease-related laboratory examinations, which also brings about the problem of a certain degree of decline in accuracy. Therefore, in order to better move towards clinical application, we still need more medical records to improve the model accuracy.

5. Conclusion

The ANN can effectively identify and differentiate patients with psoriasis, patients with CHD, and patients with psoriasis and coronary heart disease through routine examination data. It can provide dermatology clinicians with a supportive tool in the diagnostic process, providing excellent support for the diagnosis and prevention of CHD complications in patients with psoriasis.

Declarations

Author contribution statement

Ding Li, An-hai Li: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Meng-meng Qi, Li-li Yang: Contributed reagents, materials, analysis tools or data.

Wen-wen Li, Xiao-qian Yu: Analyzed and interpreted the data.

Jun Wang: Analyzed and interpreted the data; Wrote the paper.

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Data included in article/supp. material/referenced in article.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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