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Comparison of Prediction Models for Coronary Heart Diseases in Depression Patients†

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Abstract

Globally, coronary heart diseases are one of the most common diseases and regarded as a cause of deaths. Prediction and management of such diseases with high mortality as well as occurrence rate (e.g., coronary heart diseases) are particularly critical. Often, coronary heart disease patients accompany depression symptoms hence, further accurate prediction and continuing management are warranted. Improper therapeutic treatments and failure of early detection of depression patients with coronary heart diseases may result serious clinical outcomes. Data mining, utilizing database, has been shown to aid for finding effective therapeutic patterns thereby pursuing qualitative improvement of medical treatments through diagnosis based on the dataset. In the current study therefore, we compared prediction models of coronary heart disease utilizing data-mining of depression patients data in order to develop the prediction model for coronary heart diseases of depression patients. In results, we demonstrated that the neural networks model predicted most accurately thus results herein may provide a basis of prediction model for coronary heart diseases in depression patients and be effective for the establishment of effective therapeutic treatments and management plans.

Keywords*: Depression, Cardiovascular, Coronary Heart Disease, Neural Networks*

1. Introduction

People are living in the flood of information such as science, medicine, demographics, SNS in virtue of advances in technology. Such advances automatically analyze/classify/summarize information to find hidden patterns and characterize them thereby generating valuable information and searching abnormal information via analyzing patterns thereof. Ability to process and generate data has been rapidly advancing over last several decades. Increase in stored data requires new technologies to extract useful information and knowledge. Data-mining is also known as KDD (Knowledge discovery in databases) and refers to a process which extracts knowledge patterns from dataset and finds useful information. Depending upon extracted results, often future can be predicted. The prediction of diseases might be critical in reference to health management as well as for whom patients with increased life expectancy in modern times.

Large medical data may resolve issues regarding medical costs, qualitative problems of medical treatments, and their effectiveness. Data-mining is helpful as it aids doctors but also pursue qualitative improvement in medical treatments via analyzing and utilizing large database and clinical data accumulated form previous treatments and surveys thereby determining proper direction of therapeutic approaches. Data-mining, therefore

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could be an effective mean to solve various problems, medical communities are being faced.

Prediction and management of diseases are particularly critical in which such diseases represent high mortality as well as occurrence rate. Coronary heart diseases are one of the most common diseases and regarded as a cause of deaths in the world. According to the OECD Health data in 2014, the average moralities of ischemic heart disease, one of cardio-cerebrovascular and cerebrovascular disease were found to be 119.2 and 68.1 individuals, respectively that is the second highest after cancers [1]. Such diseases are not only causing pains in patients and their caregivers, yet also burdensome for nations. Coronary heart diseases are closely related with early deaths due to their critical risk and involved with mental illness such as depression. Around the developed world, represented by the United States and the European Union, there are multiple mechanistic studies undergoing in regards to association between coronary heart disease symptoms and depression. As results, it was demonstrated that most depression patients or patients with depression symptoms represented potential coronary heart disease symptoms even though they were under treatments [2].

It is critical for patients to manage their prognosis continuously as vascular diseases (*e.g.*, stroke and coronary heart diseases) often accompany depression. Serious clinical outcomes might be resulted in which early diagnosis for coronary heart diseases in depression patients, was made thereby failing proper treatments. Therefore, in the current study, we compared prediction models of coronary heart disease in depression patients utilizing data-mining of data of Korean depression patients in order to develop the prediction model for coronary heart diseases of depression patients. Prediction of coronary heart diseases in depression patients may enable the establishment of effective therapeutic treatments and management plans.

2. Health Management Algorithm Study

2.1. A Study of Depression and Coronary Heart Diseases

Depression itself is characterized with the major symptom, depressing feeling. It often causes decline in motivation, interpersonal problems and even suicide in some serious cases. Although depression may significantly impact on overall life of the individual, the rate of complete recovery is quite high hence could be effectively treated in which appropriate treatments are provided along with doctors' consultation. Therefore, depression requires continued counseling as well as psychotherapy with proper management of disease.

Coronary heart diseases indicate diseases originated from either the heart or other major blood vessels. Representative coronary heart diseases are stroke, high blood pressure, angina, and myocardial infarction. In major developed countries, the mortality of coronary heart diseases is gradually declining yet it is still considered as a major cause of death. It has been demonstrated to exacerbate symptoms thereby lowering vascular/heart functions and inducing arrhythmia. coronary heart diseases are known to be related with Social psychological risks (*e.g.*, depression and stress) hence, a number of domestic/international studies are being conducted regarding the association between depression and coronary heart diseases [3-4].

In case of Korea, there was a study investigated effects of education program of heart failure patients on their quality of life and depression [5]. Another study investigated the correlation between stroke and depression via analyzing the prevalence rate and predictors of post-stroke depression [6]. In terms of managing diseases, various studies are being actively performed in regards to improvement of life quality via development of prediction models for depression as well as coronary heart diseases [7]. Further, Yang et al., developed the prediction model to calculate risks of coronary heart disease in general population [8] while the PEI model was utilized to develop decision-making support service in order to provide personalized monitoring and guidelines [9]. There are other studies underway that are attempting to provide specific and accurate information utilizing medical data [10].

As mentioned earlier, investigations regarding the possible association between coronary heart diseases and depression have been conducted in the developed world, represented by the represented by the United States and the European Union. For instance, Musselman *et al.*, studied about the relationship of depression to cardiovascular diseases utilizing literatures from the MEDLINE database. In results, even though they were under treatments of depression (or depression symptoms), potential symptoms of cardiovascular diseases were shown in most patients [2]. In addition to results from literature review, pre-clinical animal model studies also demonstrated the biological mechanisms underlying between coronary heart diseases and depression. In the study, it was addressed that understanding the association between these diseases might be determined if simultaneous changes were observed in the repated brain system [11]. As opposed to other previous studies which lack fundamental mechanisms between these diseases, putative models were proposed with a new perspective regarding the association of depression and coronary heart diseases. In the study, the authors explained the depression and coronary heart diseases as risk factors for coronary heart diseases and depression, respectively in each model system; further fundamental processes of chronic stress in patients with depression or coronary heart diseases were also addressed via the model [12]. In addition, through the diagnosis, analysis, treatment, to management of coronary heart diseases, extensive research has been conducted regarding the coronary heart diseases as a risk factor for depression via sample surveys of patients with coronary heart diseases [13] and approaches for classification and treatments for patients with both coronary heart diseases and depression [14].

2.2. Health Management and Data-mining Study

By virtue of advances in information and communication technologies, generation and collection of data have been actively being done. Throughout overall social sectors (*e.g.*, the fields of medicine, sports, financial economics, and weather), large datasets are being created. Ease of generation and storage of a number of data proposed a novel developmental direction for data analysis. Data can be collected as much as possible without restrictions of time and place and such collected data might represent value not only as originally intended, but also for unexpected objectives. Likewise, data-mining can be defined as extraction of values, either for initially established objectives or for untargeted objective, from new and large dataset [15]. In other words, it is a process to explore and analyze a large dataset in order to find significant and meaningful trends and rules [16].

Data-mining enables doctors to find effective therapeutic patterns and to establish medical directions using large medical dataset accumulated by national institutes or hospitals so that pursuing qualitative improvement; lately, these trends are definitely noticeable in the field of academia as well as medicine [17]. Data-mining has been being merged as an effective solution to resolve current issues in the field of medicine. In this context, various approaches are being pursued in order to pursue qualitative improvements in patients' treatment in a number of investigations.

There are several typical data-mining studies proposed health management models in reference to clinical doctors' decision making systme for prediction of coronary heart diseases in depression patients [18]. Roles of data-mining have been becoming significant in not limited to diagnosis and treatments, but in aspect of health management of diseases. A typical example study was to investigate the relationships between demographic factors, measurements of quality of life, drinking and smoking habits against behaviors of health management in normal population and patients [16]. On the other hand, there was an attempt to develop a tool for measuring patients' quality of life utilizing their basic information as opposed to subjective (and possibly biased) opinion provided by patients through EQ-5D which is the typical measuring mean for [19]. In other study, Kim et al. conducted sample surveys in university students (in their twenties) to find how they trust health information and its processes achieved via social media environments; this could be a representative study that the authors provided the basis for further studies and preliminary results regarding education for patients and general public to easily access proper health information in health management [20].

Globally, the importance of data-mining, in terms of health management, is rapidly growing as well. In case of South Korea, many studies have been heavily dealt with assessment and development of prediction models which are designed for prediction and diagnosis of specific diseases utilizing medical information from national institutes and hospitals via a data-mining approach [21]. Further, attempts were frequently made to seek diagnostic and prediction methods through searching and structurization of patterns from various medical information by a data-mining approach [22-25]. A typical example includes the study predicted Alzheimer's disease using one of the data-mining approaches, the decision tree model [26]. K. Srinivas et al. also tried to predict patients with heart disease risks through a data-mining approach of medical information such as sex, age, blood pressure and blood glucose levels [27]. Another investigation also attempted to find a diagnosis method for coronary heart diseases via a fuzzy modeling which is one of the data-mining approaches [28]. Although one-sided treatment and decision making of doctors could be one of health management methods, active and aggressive willingness of patients are critical as well. In this point of view, an example includes the study of Madigan et al. investigating health management activities done at home via a data-mining approach of national institute database [29].

3. The KNHANES Dataset

In the current study, the Korea National Health and Nutrition Examination Survey (KNHANES) dataset was utilized. This dataset has been known as representative and reliable data and includes information regarding levels of public health, health awareness and behavior, food and nutrition situations at national and cities/provinces levels. The fifth edition of dataset (2010~2012) annually extracted 192 sample units from 3,800 households targeting subjects over 1 year old from January to December.

With the Rolling Survey Sampling method, the fifth KNHANES was intended to extract samples every year that exhibit similar properties as independent probability samples representing entire area. The fifth KNHANES area was extracted from 1) general housing areas generated from the lists of Korean district units (*i.e.*, Tong/Ban/Ri) and 2) apartment areas from the market price lists of apartment complexes. All survey areas were stratified with cities/provinces firstly; and then general housing areas were further stratified into 26 categories by sex and age-specific population whilst apartment areas were stratified into 24 categories by average acreage and price per each complex in advance to the data extraction. Within sample survey areas, a total of 20 households per each survey area were extracted for the analysis using the systematic extraction method. It is a consolidated national wide health and nutrition survey that consists of short term survey systems for a three-year period [30].

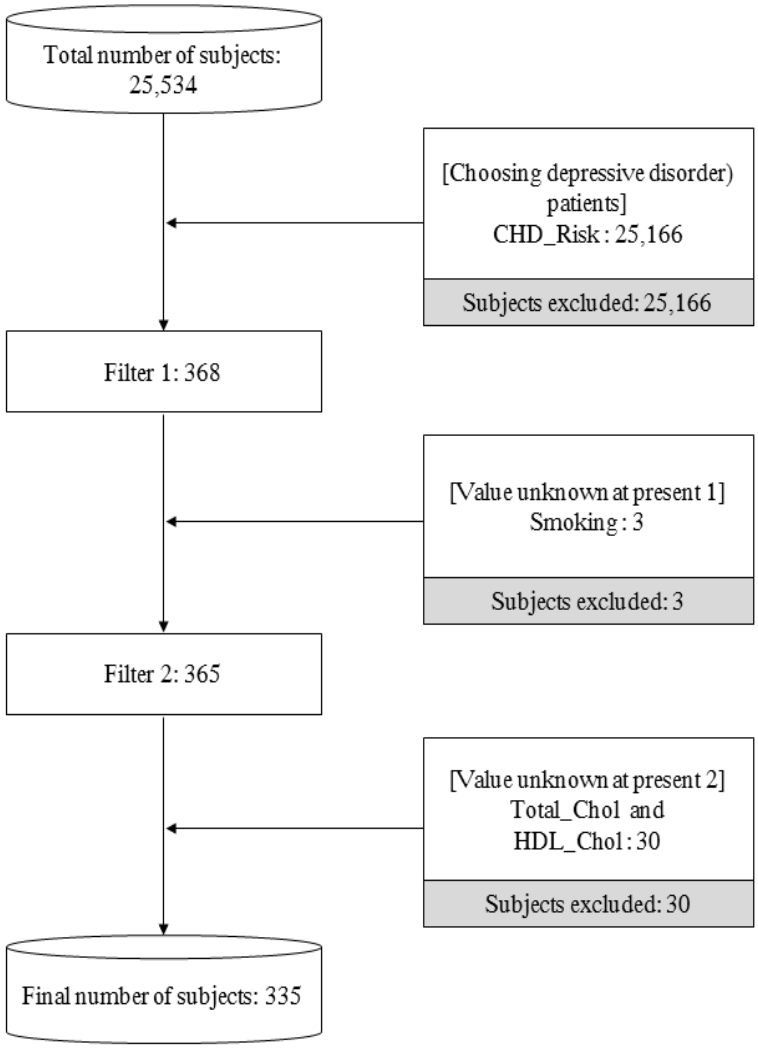

Figure 1. Data Preprocessing

In the preprocessing of data, a total of 25,534 respondents (8,958, 8,518, and 8058 respondents in 2010, 2011, and 2012, respectively) who answered at least one item of surveys was included for the study. Respondents who did not answer survey items or with missing values were excluded. Of 368 patients with depression, 3 subjects and 30 subjects were excluded as there was no response on smoking and total cholesterol/HDL cholesterol items, respectively. Therefore a total of 335 subjects were enrolled for further analysis. Subjects who 1) smoke or 2) often smoke were classified into smoking patients while subjects who 3) smoked in past yet stopped, and 8) were not applicable were converted to non-smoking patients. When it comes to diabetes mellitus, subjects who 1) did not have diabetes mellitus and 8) were not applicable converted into non-diabetes mellitus patients. For coronary heart diseases, hypertension, hyperlipidemia, stroke, myocardial infarction, and angina pectoris were investigated. Subjects were considered to have coronary heart diseases in which a patient had more than one of above diseases. The flow chart for preprocessing is depicted in the Figure 1. Final data is summarized in the Table 1. Data was randomly extracted and divided into 1) the Training data (70%; n = 226) and the Testing data (30%; n = 99) for analysis and validation.

Table 1. General Characteristics

Attributes	Types	Values	Mean
Sex	Flag	[1= Male, 2= Female]	1.81
Age	Range	[19, 82]	55.37
HDL cholesterol	Range	[13, 132]	51.11
Total cholesterol	Range	[112, 385]	194.94
Systolic blood pressure	Range	[78, 181]	121.95
Smoking	Flag	[0= Non-smoker, 1= Smoker]	0.14
Diabetes	Flag	[0 = Absent, 1 = Diabetes]	0.1
Coronary heart disease	Flag	[0 = Absent, 1 = Present]	0.38

4. Neural Networks Theory

The neural network used in the study was designed from a structure of human brain neural network and consists of processing elements (*i.e.*, neuron); although each neuron does represent slow processing speed, fast recognitions of associations and patters can be achieved via parallel transactions each other.

Of multiple neural networks, we utilized the Multi Layer Perceptron (MLP) which is one of the most common ones and is characterized with complicatedly interwinded single layer perceptrons; it can be divided into input units, hidden units, and output units. One of the characteristics of MLP is that an activation function of hidden units in the model results values only in between -1 and 1 as outputs which should be considered when applying input variables. The Back Propagation (BP) was selected as a learning algorithm in the study because 1) it is most frequently used in the MLP neural networks elsewhere and 2) minimizes errors.

The BP is widely used in various fields as it can be effectively applied in the learning of multilayer forward neuronal networks, as shown in the Figure 2. It repeats processes shown below and minimizes errors in learning. The learning processes can be classified into three steps. In the first step, learning input patterns are applied into the neural network to calculate outputs. In the following step (*i.e.*, second step), errors, defined as differences between output results and objective values, are calculated. In the third step, the error values are propagated backward and then connection weights of input units and hidden units are modified. These processes were repeated until connection weights are not modified.

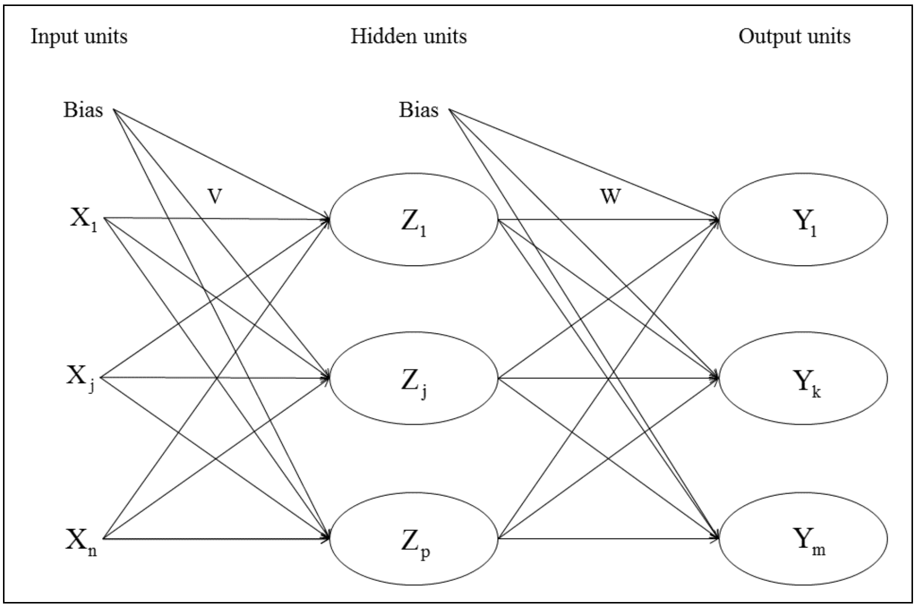

Figure 2. The Structure Map of Multilayer Forward Neural Networks

The adjustment of learning and parameters were calculated as shown in the equation (1); the input values of input units were obtained from standardized input variables, multiplied by weights and then added with threshold values.

$$I_j = \sum w_{ji} X_o + B_j \qquad (1)$$

where,

I_j : Input values

w_{ji} : Weight vector

X_o : Input unit data

B_j : Threshold value vector

Obtained input values from the equation (1) multiplied with the transfer function as shown in the equation (2) in order to result input data of hidden units

$$y_i = f(I_j) \qquad (2)$$

where,

y_i : Input data of hidden units

f : Activation function

Input data from the hidden units are multiplied by weights and then added with threshold values to calculate responsive vector and then, applied into the output units, as shown in the equation (3).

$$L_k = \sum w_{kj} y_j + B_k \qquad (3)$$

5. Experiment and Results

The Figure 3 depicts the coronary heart diseases prediction model utilizing a neural network. According to the order of importance of input values, Age, Total cholesterol, Diabetes, Systolic blood pressure, Smoking, Sex, and HDL cholesterol were subsequently subjected to algorithm calculation.

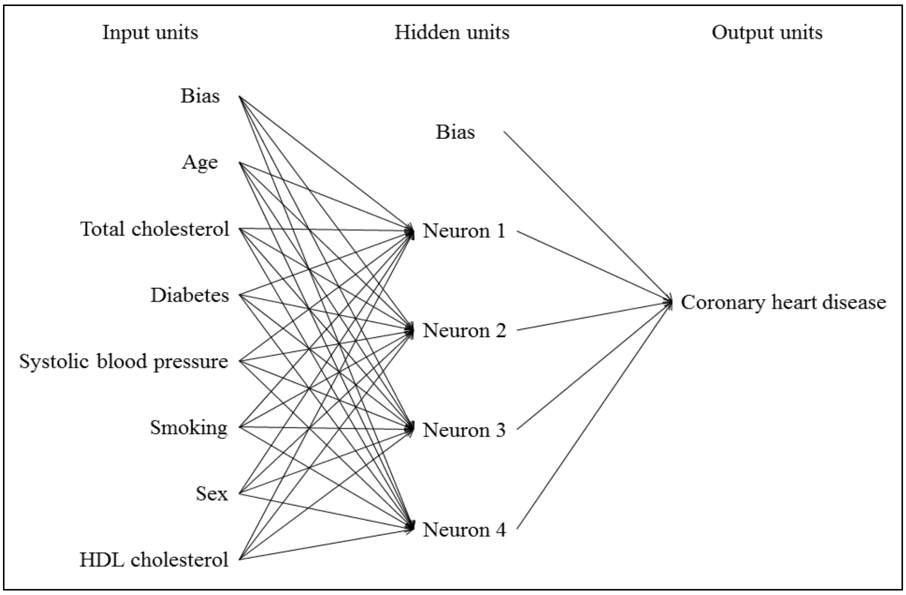

Figure 3. The Structure Map of Coronary Heart Diseases Prediction Model

In order to validate the prediction model of coronary heart diseases using a neural network, other prediction models were compared in reference to their predictive performance. For the evaluation of performance, testing data was subjected into either previous models proposed elsewhere or the model we developed.

As shown in the Figure 4, the accuracy of the prediction model we proposed herein was found to be highest (*i.e.*, 73.74% of accuracy) whilst the representative model for coronary heart diseases prediction (i.e., Framingham Risk Score; FRS) showed 64.65% accuracy which was the lowest amongst models compared. Further, this accuracy, achieved from prediction model in depression patients we developed, was higher than other models as well.

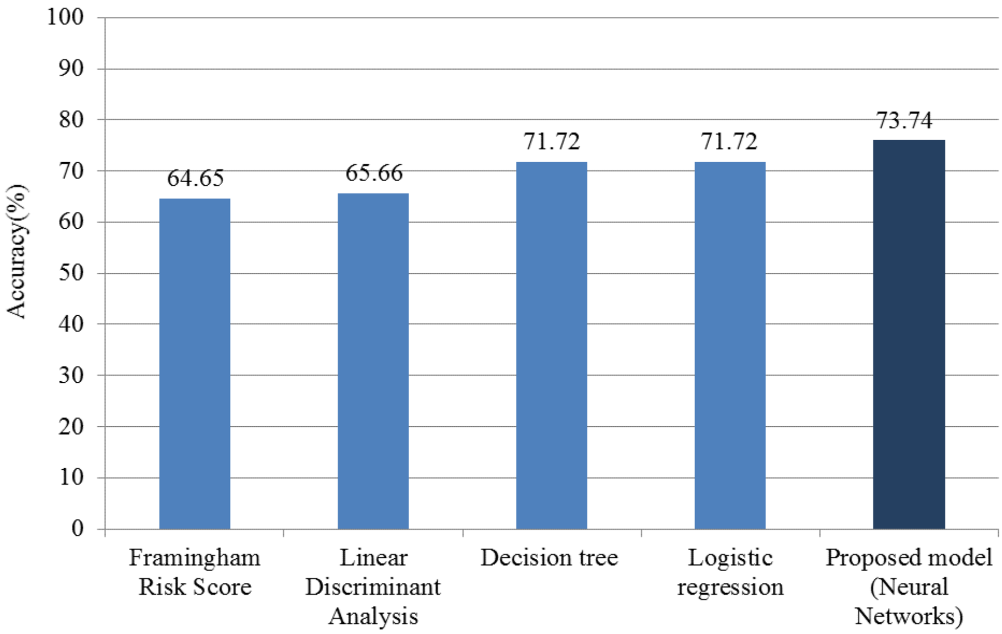

Figure 4. Comparison of Performance in Accuracy

In order to evaluate the performance of algorithms, the confusion matrix was utilized. The confusion matrix is one of the most widely utilized methods for performance evaluation and often used in the field of medicine in order to determine if one has certain disease or not. For the evaluation of algorithms, the confusion matrix (4) and Table 2 were utilized; in the Table 2, patients were classified into either 'positive response' (*i.e.*, patients with risk) or 'negative response' (*i.e.*, patients with no risk) and then sensitivity, specificity, correct proportion and miss correct proportion were calculated [32].

$$\begin{gathered} \text{Sensitivity} = TP/(TP+FN) \\ \text{Specificity} = TN/(TN+FP) \\ \text{Accuracy} = (TN+TP)/(TN+TP+FN+FP) \end{gathered} \tag{4}$$

Where, TP→True positive, TN→True negative, FN→False negative, FP→False positive

Table 2. Confusion Matrix of Sensitivity, Specificity, Accuracy

Outcome of the diagnostic test	Condition (e.g. Disease) As determined by the Standard of Truth		
	Positive	Negative	Row Total
Positive	TP	FP	TP+FP (Total number of subjects with positive test)
Negative	FN	TN	FN + TN (Total number of subjects with negative test)
Column total	TP+FN (Total number of subjects with given condition)	FP+TN (Total number of subjects without given condition)	N= TP+TN+FP+FN (Total number of subjects in study)

The Table 3 depicts the odds of correct proportion and miss correct proportion of FRS whilst the odds of proposed models in reference to correct proportion and miss correct proportion were summarized in the Table 4. The representative clinical guideline of coronary heart diseases, FRS, showed the low correct proportion (50.4%) and high miss correct proportion (49.6%, Table 3). In contrast, the proposed model, LDA-ANIFS, represented better correct proportion (68.6%) and low miss correct proportion (31.4%, Table 4).

Table 3. The Odds of Correct Proportion and Miss Correct Proportion of FRS

Correct Proportion(%)	Sensitivity	100%	51.4%
	Specificity	2.8%	
Miss Correct Proportion(%)	type I-error	0%	48.6%
	type II-error	97.2%	

Table 4. The Odds of Correct Proportion and Miss Correct Proportion of Proposed Model (Neural Network)

Correct Proportion(%)	Sensitivity	85.7%	69.2%
	Specificity	52.8%	
Miss Correct Proportion(%)	type I-error	47.2%	30.8%
	type II-error	14.3%	

The Real CHD, Risk DATA, and FRS were compared using the ROC curve as depicted in the Figure 5. The proposed neural model is shown to be close to the left top of the figure, indicating the great performance in terms of prediction of diseases. In contrast, FRS is showing the sensitivity close to 0, which indicates its non-specificity. Taken together, it can be concluded that prediction of coronary heart diseases in depression patients might be difficult.

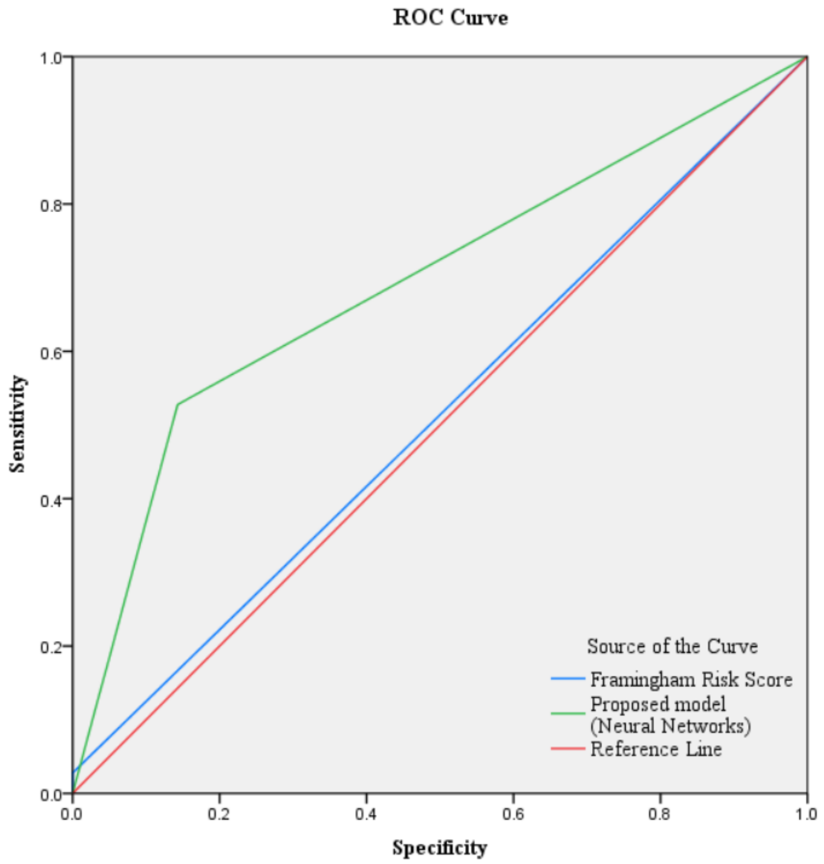

Figure 5. Comparison of ROC Curve between FRS and Neural Network Proposed in the Study

6. Conclusion

Given the prevalence of patients representing both vascular diseases (*e.g.*, stroke and coronary heart diseases) and depression, it is important for treatments to maintain patients continuously to provide continuous maintenance. Improper therapeutic treatments and failure of early detection of coronary heart diseases in depression patients may result serious problems. The FRS, the conventional prediction model for coronary heart diseases, was only able to predict one patient out of all depression patients with coronary heart diseases. The prediction of coronary heart diseases in depression patients is significantly important hence warrants the specific prediction model for it.

In the current study, we proposed the prediction model using the neural network for coronary heart diseases in depression patients and compared with other conventional models. In results, we were able to demonstrate that the proposed model herein represented the most accurate prediction compared to those of others. The prediction of diseases might be critical in reference to health management as well as for whom patients with increased life expectancy in modern times. Taken together, the present study may provide the measure for early detection of coronary heart diseases in depression thereby improving their quality of life and achieving effective health management.

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