Prediction of acute myocardial infarction with artificial neural networks in patients with nondiagnostic electrocardiogram

Javad Kojuri[1*], Reza Boostani[2], Pooyan Dehghani[3], Farzad Nowroozipour[2], Nasrin Saki[3]

[1]Cardiovascular research center, Quality Improvement in Clinical Education Research Center, Iran, Shiraz, Zand St.Namazi hospital, cardiology faculty office, Dr. Kojuri, Shiraz-Iran.

[2]Department of CSE & IT, Faculty of ECE, Shiraz University, Shiraz, Iran.

[3]Cardiovascular research center, Shiraz University of Medical Sciences, Shiraz, Iran.

ABSTRACT

Background: Myocardial infarction remains one the leading causes of mortality and morbidity and involves a high cost of care. Early prediction can be helpful in preventing the development of myocardial infarction with appropriate diagnosis and treatment. Artificial neural networks have opened new horizons in learning about the natural history of diseases and predicting cardiac disease. **Methods:** A total of 935 cardiac patients with chest pain and nondiagnostic electrocardiogram (ECG) were enrolled and followed for 2 weeks in two groups based on the appearance of myocardial infarction. Two types of data were used for all patients: nominal (clinical data) and quantitative (ECG findings). Two different artificial neural networks – radial basis function (RBF) and multi-layer perceptron (MLP) – were used to classify the two groups. **Results:** The RBF neural network had an accuracy of 83% with ECG findings and an accuracy of 78% with clinical features. When and clinical data were used in an MLP neural network trained with a genetic algorithm, ECG results led to a classification accuracy of 96% and clinical data yielded an accuracy of 84.5%. **Conclusion:** Both neural network structures predicted MI within about 2 weeks of hospital referral with an acceptable degree of accuracy in patients with nondiagnostic ECG. The MLP neural network significantly outperformed the RBF network because of the use of the genetic algorithm, which provided a global strategy to accurately determine MLP weights (clinical trials registry: NCT01870258).

Key words: Artificial neural networks, Electrocardiography, Myocardial infarction**,** Multi-layer perceptron (MLP), Radial basis function (RBF).

INTRODUCTION

Atherosclerosis is one of the leading causes of death in the world. Moreover, it is the main cause of coronary artery disease (CAD), a progressive disease that causes atherosclerotic changes in the coronary artery walls and usually appears in mid- to late adulthood.[1]

Acute myocardial infarction, involving irreversible necrosis of heart muscle secondary to prolonged ischemia, is the most deadly presentation of CAD. Infarction usually arises from an imbalance between oxygen supply and demand, which is most often caused by plaque rupture and thrombus formation in a coronary vessel, leading to an acute reduction in the blood supply to a portion of the myocardium.[2] Myocardial infarction may lead to systolic or diastolic dysfunction and may increase the predisposition to arrhythmias and other complications such as ischemic, mechanical, embolic and inflammatory disturbances.[3] Because of the high cost of care, effective drugs and treatments, the prevention of myocardial infarction is a desirable goal. To predict the likelihood of myocardial infarction many factors have been used, such as laboratory data, history and physical examination findings; some of the results have been hopeful but none of these studies were successful in accurately predicting the likelihood of

***Corresponding address:**
Prof. Javan Kojuri
Cardiovascular research center, Iran, Shiraz, Zand St.Namazi hospital, cardiology faculty office, Dr. Kojuri, Shiraz-Iran.
E mail: Kojurij@yahoo.com

DOI: 10.5530/jcdr.2015.2.2

myocardial infarction.[4,5]

Artificial neural networks (ANN) have been widely used in various fields such as function approximation, prediction, modeling and classification, and they have the potential to open new prospects in managing cardiac problems such as disease prediction, diagnosis and classification of diseases with similar signs and symptoms.[6] It should be noted that ANN have been repeatedly used in different medical fields.[7,8]

In the field of cardiology,[9] ANN have been successfully applied to the diagnosis and treatment of CAD and myocardial infarction,[10,11,12] electrocardiogram (ECG) interpretation, the detection of arrhythmias[13] and especially in the analysis of ECG images.[14] Many studies have reported positive results for the detection of myocardial infarction from 12-lead ECG (with better accuracy than an expert cardiologist),[15] the early diagnosis of myocardial infarction, and the prediction of infarct size in patients with chest pain.[16]

Given the importance of preventing myocardial infarction and because of the lack of studies designed to test methods of prediction, this study aimed to compare the ability of two ANN-based approaches to predict myocardial infarction within 2 weeks in patients with chest pain.

MATERIALS AND METHODS

Study sample

Our study sample consisted of all 964 patients with chest pain referred to Fateme Alzahra Hospital between October 2011 and April 2012 with nondiagnostic ECG at the time of referral who met the following criteria:

- Absence of a history of myocardial infarction,
- Absence of bundle branch block, Wolf-Parkinson-White abnormality, ventricular hypertrophy or previous ECG signs of myocardial infarction,
- Absence of a history of percutaneous coronary surgery or coronary artery bypass grafting,
- Absence of ECG abnormalities attributable to drugs such as digoxin or tricyclic antidepressants.

The ECGs were recorded with Cardiax (SOT Sonotechnik, Maria Rain, Austria) setup interfaced to a computer. The raw ECG signals were analyzed with Cardiax version 3.50 Beta 4 software, a computer-aided instructional program. Heart rate, QRS axis, QRS duration, QT and QTc interval, ST segment deviations and T wave amplitude in all of the 12 leads were calculated by the software, and were considered as input feature vectors within each time frame for the ANN. All patients were followed up for 2 weeks and separated into two groups based on the occurrence of myocardial infarction. Myocardial infarction was defined as a typical rise or fall in biomechanical markers of myocardial necrosis with at least one of the following:

- Ischemic symptoms
- Appearance of pathologic Q waves on ECG
- Electrocardiographic changes indicative of ischemia (ST segment elevation or depression)
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Group 1 included patients who had a myocardial infarction within the 2-week follow-up period, and group 2 included patients who did not have a myocardial infarction during this period. For all patients we recorded clinical information including history, physical examination, laboratory tests and ECG at the time of presentation. This information was used as feature vectors for input in the ANN. In addition, anxiety scores calculated with the Hamilton Anxiety Scale were recorded. All patients filled the written consent. The study protocol was approved by ethics committee of faculty of research of Shiraz University of Medical sciences with the referral number of: 3106

Electrocardiographic diagnosis

The ECGs were recorded with a Cardiax device interfaced with a computer and analyzed with Cardiax software version 3.50 Beta 4 software, a computer-aided instructional program. Heart rate, QRS axis, QRS duration, QT and QTc interval, ST segment deviations and T wave amplitude in all 12 leads were calculated by the software, named as group 1 and used as inputs in the neural networks. The first group (dataset 1) included 82 patients who presented with myocardial infarction and 853 patients (dataset 2) for whom myocardial infarction was not recorded during a 3-month follow-up period.

Clinical diagnosis

All of the patients' data including history, physical examination, laboratory tests and ECG findings were used as dataset 2 for the ANN. These clinical data were used for 82 patients who presented with myocardial infarction and

Table 1: Patient's clinical data for history, physical examination and laboratory tests

Name	**Gender**	**Age**
Tel	**Code**	
Main presenting symptoms		
Ischemic type (typical) chest pain □ Atypical chest pain □ Dyspnea □ Cold sweats □ Nausea/Vomiting □ Weakness □ Palpitation □ Dizziness/Syncope □ Aborted SCD or Cardiac arrest □ Other:		
Risk factors		
Diabetes mellitus □ Hypertension □ Dyslipidemia □ IHD □ Kidney disease □ Peripheral artery disease □ Family history of premature CAD □ Cigarette smoking □ Water pipe smoking □ Opium □ Anxiety score: Mild anxiety (14-17) □ Moderate Anxiety (18-24) □ Severe anxiety (25-30) □		
Family history		
Past cardiac history		
Physical examination		
Blood pressure: Heart rate: Pulmonary edema: □ Peripheral edema: □		
Laboratory data		
Wbc: Hb: Plt: Bun: Creat: Na: K: FBS: TG: Chol: LDL: HDL: CPK-MB:		
Echocardiography		
LVEF: RWMA:		
Angiography (If done)		

853 patients who did not have myocardial infarction. The form used to record clinical data is shown in Table 1. Anxiety scores were calculated with the Hamilton Anxiety Scale.

Description of the artificial neural network algorithms

Multi-layer perceptron

The ANN classifier used for the multi-layer perceptron (MLP) network in this study is a standard feed-forward system containing a single hidden layer and a back-propagation training algorithm Figure 1. Each input neuron is connected to a hidden neuron, and all neurons subsequently connect to the output neuron. Each input neuron receives a numerical input from all input features, which are normalized within an interval of 0 to 1. These values are then multiplied by the connection weights, which represent the relative influences between the neurons from the first layer to the next one. These multiplications are summed and passed through the network. The most common activation function is the sigmoid function, which simulates the all-or-none behavior of biological neurons. The outputs of the hidden neurons are then multiplied by the appropriate connection weights and fed to the last decision-maker neuron. The output neuron performs identical calculations to produce the final output of the network.[17] We selected the optimal number of hidden neurons that would result in a predictive network with maximal sensitivity and specificity.

Radial basis function network model

The radial basis function (RBF) network has a feed-forward structure consisting of a single hidden layer containing J locally tuned units, which are fully interconnected to an output layer containing a decision-maker neuron. It should be noted that the hidden neurons are more biased to the central data located around the centers. All hidden units simultaneously receive the n-dimensional real value input vector X as shown in Figure 2.

Radial bias function networks can be used for regression and pattern classification tasks. The RBF network has three layers in which the first layer consists of receptor neurons and the hidden layer usually contains several neurons with a Gaussian activation function. In fact, Gaussian neurons comprise a set of receptive fields that model the input spaces. For Gaussian RBF this sensitivity can be tuned by adjusting the spread parameterσ, where a larger spread

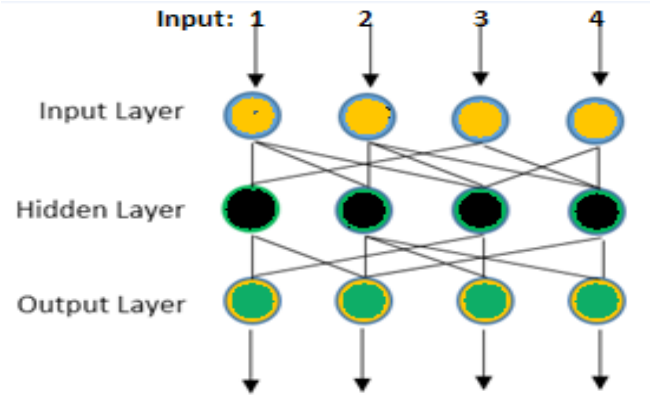

Figure 1: Feed forward neural network showing unidirectional movement of the information

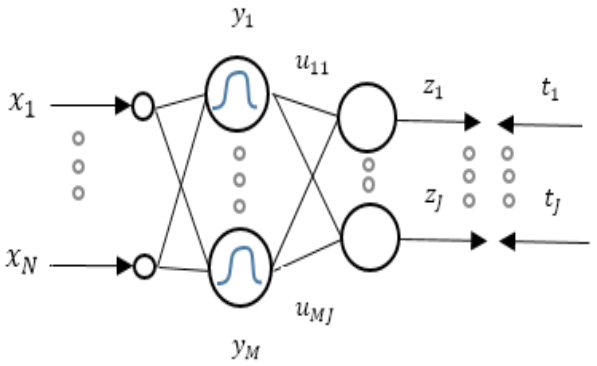

Figure 2: Radial basis function neural network

implies less sensitivity.

The output of a RBF network is described according to Eq. (1):

$$f(X) = W_0 + \sum_{i=1}^{m} W_i \varphi_i(X) \quad \varphi_i(X) = e^{-\frac{\|X - C_i\|^2}{r_i^2}} \qquad (1)$$

The main structural difference between RBF and MLP networks is the absence of weights in first hidden layer. In other words, the hidden-unit outputs are not calculated with the weighted-sum mechanism and sigmoid activation. One of the fastest and most accurate learning algorithms for this network is termed the "fixed center point", in which only the final layer weights are trained.[18-20]

Evaluation Scheme

To enhance the performance of the MLP network, we used a genetic algorithm instead of a gradient descent algorithm. Average classification error was calculated for each batch.[18] Diagnostic performance was estimated with ten-fold cross-validation in which each round considered 90% of the instances as the training sample and the remaining 10% as the test sample. The place of training and test sets were repeated 10 times; each time 10% of the data was considered the test sample and the remaining 90% was used as the training sample. This process was repeated 10 times, and each time the entire body of data was permutated to merge the dataset. To ensure the results were robust, the averafge of these 100 experiments was reported as the

Table 2: Summary of patients' demographic data and clinical history

	All patients	Patients with MI	Patients without MI	P value
Mean age (years)	57.07	59.5	56.85	0.231
Male	408 (43.63%)	56 (71.79%)	352 (41.07%)	0.0001
Female	527 (56.36%)	22 (28.20%)	505 (58.92%)	0.0001
Typical chest pain	409 (43.74%)	69 (88.46%)	340 (39.67%)	0.0003
Atypical chest pain	526 (56.25%)	9 (11.53%)	517 (60.32%)	0.0003
Dyspnea	513 (54.86%)	30 (38.46%)	483 (56.35%)	0.007
Cold sweats	233 (24.91%)	36 (46.15%)	197 (22.98%)	0.001
Nausea/Vomiting	205 (21.92%)	39 (50%)	165 (19.20%)	0.0002
Weakness	73 (7.80%)	7 (8.97%)	66 (7.70%)	0.119
Dizziness	141 (15.08%)	9 (11.53%)	132 (15.40%)	0.05
Palpitations	133 (14.22%)	3 (3.84%)	130 (15.16%)	0.017
Diabetes mellitus	143 (15.29%)	22 (28.20%)	121 (14.11%)	0.027
Hypertension	373 (39.89%)	33 (42.30%)	340 (39.67%)	0.503
Hyperlipidemia	151 (16.14%)	30 (38.46%)	121 (14.11%)	0.001
Ischemic heart disease	163 (17.43%)	20 (25.74%)	143 (16.68%)	0.166
Smoking	281 (30.05%)	39 (50%)	242 (28.23%)	0.0001
Opium use	73 (7.80%)	18 (23.07)	55 (6.41%)	0.008
Family history	81 (8.66%)	15 (19.23%)	66 (7.70%)	0.013
Anxiety score	15.29	15.08	15.31	0.398

Table 3: Laboratory data for patients at presentation

	All patients	Patients with MI	Patients without MI	P value
White blood cells [cells/mm3]	8521	10148	8373	0.05
Hemoglobin [g/dL]	13.24	13.86	13.18	0.06
Platelets [cells/mm3]	233387	232731	233447	0.848
Blood urea nitrogen [mg/dL]	17.99	17.19	18.07	0.836
Creatinine [mg/dL]	1.09	1.03	1.10	0.080
Sodium [mEq/L]	139.39	139.50	139.38	0.418
Potassium [mEq/L]	4.51	4.06	4.55	0.441
Blood sugar [mg/dL]	123.09	138.21	121.71	5.6
Triglycerides [mg/dL]	147.37	172.37	145.09	5.2
Total cholesterol [mg/dL]	166.16	189.52	164.03	3.8
LDL [mg/dL]	97.20	118.14	95.30	2.87
HDL [mg/dL]	37.50	36.75	37.57	0.864

mean classification rate with standard deviation for all 100 values. To optimize the network topology, this procedure was used for different numbers of neurons and the one that performed best was selected as the desired topology. The resulting network was able to control the trade-off between over-fitting and generalization in both MLP and RBF networks.[21,22]

Statistical Methods

To evaluate the performance of the neural net works, paired t-tests were first used to detect significant differences. The F-test was then used to identify separable clusters of data in the feature space. For each comparison we calculated the P value; next, we calculated the confusion matrix for each network to assess sensitivity and specificity. These values illustrate how well the network balances the trade-off between sensitivity and specificity factors. In addition, positive predictive value (PPV) and negative predictive value (NPV) were determined.

RESULTS

Patient characteristics

The incidence of myocardial infarction in patients with chest pain and nondiagnostic ECG at presentation was 8.34%. Table 2,3 summarizes the patients' demographic and clinical data. Mean heart rate was 78.27 bpm and mean blood pressure was 130.99/80.45 mm Hg for the whole sample of patients; these values were 76.96 bpm and 136.28/83.41 mm Hg for group 1, and 78.39 bpm and 130.51/80.19 mm Hg for group 2.

Improvement in MLP performance with the genetic algorithm

To achieve acceptable performance with the MLP network, a genetic optimization algorithm is used to explore the solution space to avoid being trapped in a local minimum. Figures 3 and 4 show the average distance between

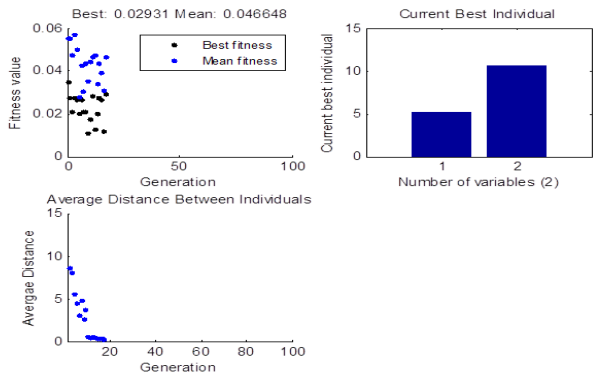

Figure 3: Average distance between individuals, best fit and current individuals in an MLP neural network with two hidden layers (dataset 1)

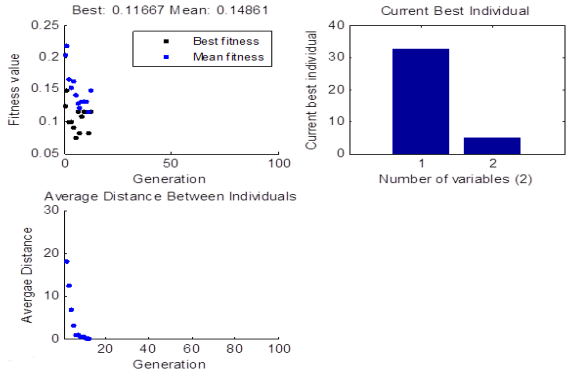

Figure 4: Average distance between individuals, best fit and current best individuals in the MLP neural network with two hidden layers (dataset 2)

Table 4: Classification rate, sensitivity, specificity, positive predictive value and negative predictive value for the RBF neural network with dataset 1 (ECG data)

	Classification rate (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Training phase	90.14 (± 0.08)	97.29	83	99.62	41.78
Test phase	82.76	80	85.52	97.64	36.36

Table 5: Classification rate, sensitivity, specificity, positive predictive value and negative predictive value for the RBF neural network with dataset 2 (history, physical examination andlaboratory tests)

	Classification rate (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Training phase	84.71(± 0.13)	81.57	87.86	84.82	88.42
Test phase	78	68.75	86.67	72.22	84.62

Table 6: Classification rate, sensitivity, specificity, positive predictive value and negative predictive value for the MLP neural network with dataset 1 (ECG data)

	Classification rate (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Training phase	0.9728 (± 0.04)	95.33	99.22	99.66	95.10
Test phase	95.63	93.33	97.93	99.30	82.35

Table 7: Classification rate, sensitivity, specificity, positive predictive value and negative predictive value for the MLP neural network with dataset 2 (history, physical examination and laboratory tests)

	Classification rate (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Training phase	88.75 (± 0.13)	88.50	89	95.24	94.32
Test phase	84.17	75	93.33	82	100

individuals, fitness values and the best candidates for the MLP weights obtained with datasets 1 and 2, respectively. With dataset 1, the best MLP network comprised two hidden layers containing 6 and 11 neurons. Figure 4 shows the same process for dataset 2; in this case the best network comprised two hidden layers with 33 and 6 neurons.

Diagnostic indicators of myocardial infarction identified with ANN algorithms

Both the RBF and especially the MLP networks successfully classified ECG results consistent with the clinical data. The RBF network achieved a successful classification rate or accuracy (defined as the total number of correct diagnoses in patient with and without myocardial infarction divided by the total number of patients) of 90.14%, with 97.29% sensitivity and 83% specificity for the training phase, and 80% sensitivity and 85.52% specificity for the test phase (Table 4). For the clinical data, the training phase showed 81.57% sensitivity, 87.56% specificity, 73% PPV and 98% NPV and the test phase showed 68.75% sensitivity, 86.47% specificity, 72.22% PPV and 84.62% NPV (Table 5).

The MLP neural network performed even better than the RBF network. With the ECG results, sensitivity was 95.33%, specificity was 99.22%, PPV was 99.66% and NPV was 95.1% for the training phase, and these values were 93.33%, 97.93%, 99.3% and 82.35% respectively for the test phase (Table 6).

With the clinical dataset, the MLP network yielded a sensitivity of 88.75%, a specificity of 88.5%, a PPV of 95.24% and a NPVof 94.32% for the training phase; the values for the test phase were 75%, 93.33%, 82% and 100%, respectively (Table 7). Figures 5 and 6 show that the MLP network outperformed the RBF network with both the ECG and clinical data.

We compared the performance of two well-known neural networks, MLP and RBF, in predicting acute myocardial infarction in patients with chest pain and nondiagnostic ECG within 2 weeks after their referral to the hospital. The radial basis function (RBF) network has a feed-forward structure consisting of a single hidden layer containing J locally tuned units, which are fully interconnected to an output layer containing a decision-maker neuron. The

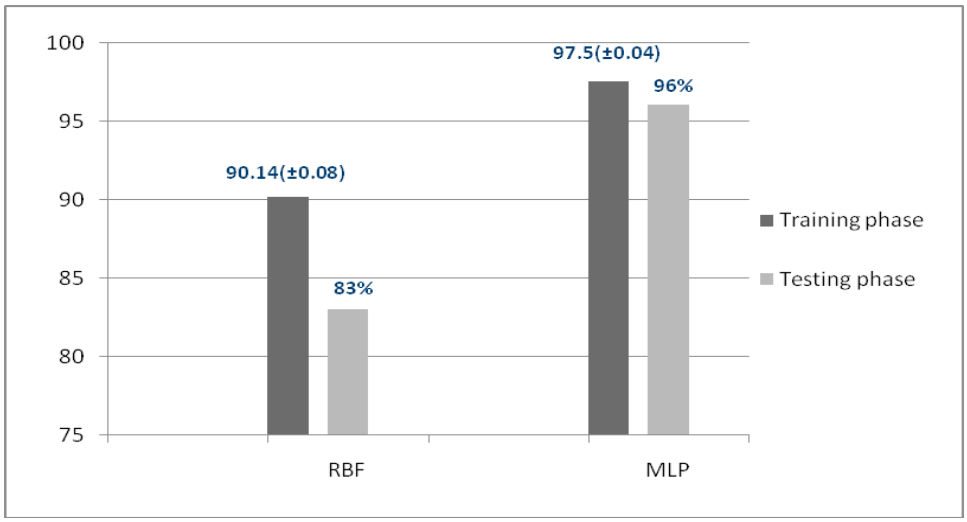

Figure 5: Final comparison of the performance of MLP and RBF neural networks with ECG data

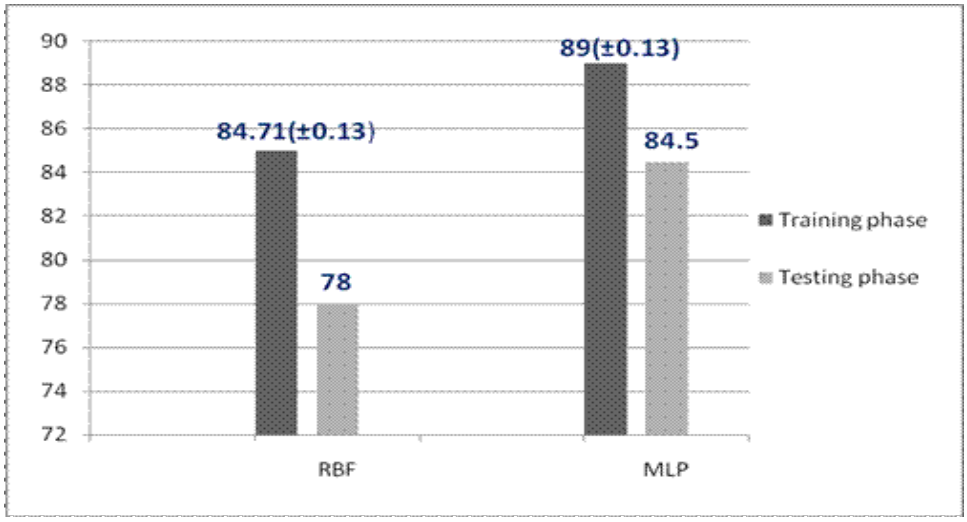

Figure 6: Final comparison of the performance of MLP and RBF neural networks with history, physical examination and laboratory test data

ANN classifier used for the multi-layer perceptron (MLP) network in this study is a standard feed-forward system containing a single hidden layer and a back-propagation training algorithm. Each input neuron is connected to a hidden neuron, and all neurons subsequently connect to the output neuron. Each input neuron receives a numerical input from all input features, which are normalized within an interval of 0 to 1. Classification with MLP faces two challenges: first, determining suitable weights to avoid being trapped in a local minimum and second, choosing the number of layers and the number of neurons within each layer. The performance of an MLP network is sensitive to its initial weights; this challenge is greater than the correct choice of the number of layers and neurons. Regarding the ability of the genetic algorithm to control the trade-off between exploration and exploitation, a population of initial weights is expected to be better able to explore the search space, and to result in acceptable weights for the network. This challenge is also present in the RBF network, where the weights of the second layer to the final decision neuron must be trained; consequently, the same procedure as for the RBF structure was used to find suitable weights to enhance the performance of RBF networks.

According to the universal approximation theorem, an MLP is capable of approximating any smooth nonlinear input-output mapping to an arbitrary degree of accuracy if and only if a sufficient number of hidden layer neurons are used. Because the boundary between features in the two classes in this study is a flexible hyper-plane, the MLP network with one hidden layer is able to estimate this hyper-plane with acceptable accuracy. Moreover, it

has been shown that MLP networks are able to model RBF networks when the two networks are fairly similar in complexity; in other words, both benefit from a single hidden layer although the number of neurons in this layer can be different.[23] The main reason for choosing one network rather than the other is based on its learning performance with a given dataset. Our results showed that the MLP network outperformed the RBF network, most likely because of the latter's greater sensitivity to the high dimensionality of the input vectors (e.g. clinical data) compared to the MLP network.[24-26]

The ability of the MLP neural network to predict myocardial infarction in accordance with clinical data was acceptable, and further studies may demonstrate the efficiency of this model compared to other models. An ANN may be particularly useful when the primary goal is classification and regression; it can also be useful when interactions or complex nonlinearities exist in the dataset.[23,28,29]

The differences in outputs between the MLP and RBF networks reflect the deviation from a Gaussian distribution in both datasets, because our datasets obeyed a non-Gaussian distribution. Because the RBF network contains several Gaussian functions, each characterized by a certain mean vector along with a covariance matrix, it is able to model every arbitrary distribution. However, if the data are distributed in a highly asymmetric way, a large number of Gaussian neurons is needed, and this can lead to the oversetting dilemma. In other words the RBF network is a good local approximator, whereas the MLP network is a strong general approximator.[30]

The generalization properties of a neural network can be documented by measuring the distance between training and testing error, and by considering the standard deviations around the mean values. The closer these two values are to each other, the better the generalization can be assumed to be in empirical terms. Moreover, good generalization ensures that over-fitting has not occurred.[31,32]

CONCLUSION

The ability to predict myocardial infarction would be a breakthrough in the field of cardiology, but to date there is no reliable method for this. Our results showed that even the presence of more risk factors and higher anxiety scores, and recent repeat angina attacks, cannot reliably predict future myocardial infarction. This study compared the ability of two types of ANN (MLP and RBF) to correctly predict myocardial infarction in two groups of patients on the basis of clinical data and ECG findings. The MLP network outperformed the RBF network in terms of accuracy and generalization. As a result, commercial software with a user-friendly graphic user interface has been installed at a pilot hospital and is being evaluated with ECG and clinical data as a tool to predict acute myocardial infarction within the subsequent 2 weeks in patients presenting with chest pain and no diagnostic ECG. This method could be applied to other fields of medical diagnosis by choosing a suitable network and the most appropriate clinical data depending on the disease or condition of interest. Methods based on an ANN may be especially useful when the decision of a specialist carries a high degree of uncertainty.

STUDY LIMITATIONS

One of the limitations of our study was that only 82 of our patients had myocardial infarction during the 2-week study period. This limited number of MI cases may be the reason that ppv of MLP group was pretty high. To overcome this problem further multicenter studies with larger sample sizes are needed. By the way, data collection of our study is going on and we aim to extend our sample size in the near future.

CONFLICT OF INTEREST

We, Javad Kojuri, Reza Boostani, Pooyan Dehghani, Farzad Nowroozipour, Nasrin Saki, authors of this study confirmed that none of us has not any conflict of interest.

ACKNOWLEDGMENTS

This work was supported by the research faculty of Shiraz University of Medical Sciences and Shiraz University. We thank K. Shashok (Author AID in the Eastern Mediterranean) for improving the use of English in the manuscript.

REFERENCES

1. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005 Apr 21; 352(16): 1685-95.
2. Davì G, Patrono C. Platelet activation and atherothrombosis. N Engl J Med. 2007 Dec 13; 357(24): 2482-94.
3. Mullasari AS, Balaji P, Khando T. Managing complications in acute myocardial infarction. J Assoc Physicians India. 2011 Dec; 59 Suppl(1): 43-8.
4. Karlson BW, Herlitz J, Wiklund O, Richter A, Hjalmarson A. Early prediction of acute myocardial infarction from clinical history, examination and electrocardiogram in the emergency room. Am J Cardiol. 1991 Jul 15; 68(2): 171-5.
5. Mocan T, Agoşton-Coldea L, Gatfossé M, Rosenstingl S, Mocan LC, Dumitraşcu DL. A new prediction score for myocardial infarction: MINF SCORE. Rom J Intern Med. 2008; 46(2): 145-51.
6. Shuffle barger CM. What is a neural network? Ann Emerg Med. 1992 Dec; 21(12): 1461-2.
7. Pandey B, Mishra RB. Knowledge and intelligent computing system in medicine. Comput Biol Med. 2009 Mar; 39(3): 215-30.
8. Al-Shayea QK. Artificial Neural Networks in Medical Diagnosis. IJCSI International Journal of Computer Science 2011 Mar; 8(2): 150-4.
9. Itchhaporia D, Snow PB, Almassy RJ, Oetgen WJ. Artificial neural networks: current status in cardiovascular medicine. J Am Coll Cardiol. 1996 Aug; 28(2): 515-21.
10. Baxt WG, Shofer FS, Sites FD, Hollander JE. A neural network aid for the early diagnosis of cardiac ischemia in patients presenting to the emergency department with chest pain. Ann Emerg Med. 2002 Dec; 40(6): 575-83.
11. Hedén B, Edenbrandt L, Haisty WK Jr, Pahlm O. Artificial neural networks for the electrocardiographic diagnosis of healed myocardial infarction. Am J Cardiol. 1994 Jul 1; 74(1): 5-8.
12. Mobley BA, Schechter E, Moore WE, McKee PA, Eichner JE. Predictions of coronary artery stenosis by artificial neural network. Artif Intell Med. 2000 Mar; 18(3): 187-203.
13. Dallali A, Kachouri A, Samet M. Integration of HRV, WT and neural networks for ECG arrhythmias classification. ARPN Journal of Engineering and Applied Sciences 2011 May; 6(5): 74-82.
14. McMahon EM, Korinek J, Yoshifuku S, Sengupta PP, Manduca A, Belohlavek M. Classification of acute myocardial ischemia by artificial neural network using echocardiographic strain waveforms. Comput Biol Med. 2008 Apr; 38(4): 416-24.
15. Hedén B, Ohlin H, Rittner R, Edenbrandt L. Acute myocardial infarction detected in the 12-lead ECG by artificial neural networks. Circulation 1997 Sep 16; 96(6): 1798-802.
16. Eggers KM, Ellenius J, Dellborg M, Groth T, Oldgren J, Swahn E, Lindahl B. Artificial neural network algorithms for early diagnosis of acute myocardial infarction and prediction of infarct size in chest pain patients. Int J Cardiol. 2007 Jan 18; 114(3): 366-74.
17. Mobley BA, Schechter E, Moore WE, McKee PA, Eichner JE. Neural network predictions of significant coronary artery stenosis in men. Artif Intell Med. 2005 Jun; 34(2): 151-61.
18. Xue J, Aufderheide T, Scott Wright R, Klein J, Farrell R, Rowlandson I, Young B. Added value of new acute coronary syndrome computer algorithm for interpretation of prehospital electrocardiograms. J Electrocardiol. 2004; 37 Suppl(1): 233-9.
19. Wallis JW. Use of artificial intelligence in cardiac imaging. J Nucl Med. 2001 Aug; 42(8): 1192-4.
20. DeGroff CG, Bhatikar S, Hertzberg J, Shandas R, Valdes-Cruz L, Mahajan RL. Artificial neural network-based method of screening heart murmurs in children. Circulation 2001 Jun 5; 103(22): 2711-6.
21. Atkov OY, Gorokhova SG, Sboev AG, Generozov EV, Muraseyeva EV, Moroshkina SY, *et al*. Coronary heart disease diagnosis by artificial neural networks including genetic polymorphisms and clinical parameters. J Cardiol. 2012 Mar; 59(2): 190-4.
22. Baxt WG. Analysis of the clinical variables driving decision in an artificial neural network trained to identify the presence of myocardial infarction. Ann Emerg Med. 1992 Dec; 21(12): 1439-44.
23. Liu T, Wang Q, Baxter MS, Sayre MR, Gilber WB. Development of a statistical model for prediction of acute myocardial infarction by biochemical markers. Drug Inf J. 1999 Jan; 33(1): 141-8.
24. Haraldsson H, Edenbrandt L, Ohlsson M. Detecting acute myocardial infarction in the 12-lead ECG using Hermite expansions and neural networks. Artif Intell Med. 2004 Oct; 32(2): 127-36.
25. Awais MM, Awas SK. Gastro-intestinal tract inspired computational model for myocardial infarction diagnosis. Expert Sys Appl. 2011 May; 38(5): 5633-41.
26. Hollander JE, Sease KL, Sparano DM, Sites FD, Shofer FS, Baxt WG. Effects of neural network feedback to physicians on admit/discharge decision for emergency department patients with chest pain. Ann Emerg Med. 2004 Sep; 44(3): 199-205.
27. Harrison RF, Kennedy RL. Artificial neural network models for prediction of acute coronary syndromes using clinical data from the time of presentation. Ann Emerg Med. 2005 Nov; 46(5): 431-9.
28. Forberg JL, Green M, Björk J, Ohlsson M, Edenbrandt L, Ohlin H, *et al*. In search of the best method to predict acute coronary syndrome using only the electrocardiogram from the emergency department. J Electrocardiol. 2009 Jan-Feb; 42(1): 58-63.
29. Ariet M, Zhou S, DeLuca DC, Greenfield JC Jr. Computerized serial comparison of electro cardiograms: program performance in myocardial infarction. J Electrocardiol. 2007 Apr; 40(2): 147-54.
30. Christenson J, Innes G, McKnight D, Thompson CR, Wong H, Yu E, *et al*. A clinical prediction rule for early discharge of patients with chest pain. Ann Emerg Med. 2006 Jan; 47(1): 1-10.