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The Prediction of the Risk Level of Pulmonary Embolism and Deep Vein Thrombosis through Artificial Neural Network

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ABSTRACT

Background: Venous thromboembolism is a common cause of mortality among hospitalized patients and yet it is preventable through detecting the precipitating factors and a prompt diagnosis by specialists. The present study has been carried out in order to assist specialists in the diagnosis and prediction of the risk level of pulmonary embolism in patients, by means of artificial neural network. **Method:** A number of 31 risk factors have been used in this study in order to evaluate the conditions of 294 patients hospitalized in 3 educational hospitals affiliated with Kerman University of Medical Sciences. Two types of artificial neural networks, namely Feed-Forward Back Propagation and Elman Back Propagation, were compared in this study. **Results:** Through an optimized artificial neural network model, an accuracy and risk level index of 93.23 percent was achieved and, subsequently, the results have been compared with those obtained from the perfusion scan of the patients. 86.61 percent of high risk patients diagnosed through perfusion scan diagnostic method were also diagnosed correctly through the method proposed in the present study. **Conclusions:** The results of this study can be a good resource for physicians, medical assistants, and healthcare staff to diagnose high risk patients more precisely and prevent the mortalities. Additionally, expenses and other unnecessary diagnostic methods such as perfusion scans can be efficiently reduced.

Key words: Venous thromboembolism, Pulmonary Embolism, Deep Vein Thrombosis, Risk Factors, Artificial Neural Network

1. INTRODUCTION

The condition of Venous Thromboembolism (VTE) which is one of the main causes of mortalities in the world includes Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT). PE which is the lethal form of VTE. The annual incidence rates of VTE among people of European ancestry estimate from 104 to 183 per 100,000 person-years (1). A number of 50 to 75 percent of VTE cases occur in surgical ward and ICUs of hospitals. The majority of the patients hospitalized in intensive care units (ICUs) are highly at risk of the incidence of VTE due to being immobilized or suffering from background diseases (2). Also in Iran, VTE in hospitalized patients was 9 per 10000 and 11 percent mortality (3). The average annual number of total adult patients with predisposing conditions of DVT in Iran was 5,288,272 people. The mean annual prevalence rate of DVT among the hospitalized Iranian adult patients with the risk of DVT was approximately between 129.90 and 395.16 cases per 1000 patients (4). A considerable number of PEs and DVTs are currently occurring in internal medicine, orthopedics, surgery and gynecology wards that appear to be preventable (5-9) though we did not notice any plans to either prevent or reduce the number of these cases in Iran. According to some reports as well as other reports pertaining to a number of studies, preventive measures are being taken for a very small percentage of post surgical patients with the potential of VTE (3-4, 10).

In current decades, the application of Artificial Neural Network (ANN) have turned out to be highly effective in analyzing, modeling, and determining the relations existing in the medical data (11-15). The results of a number of studies indicate that the application of ANN method can help physicians with the clinical diagnosis and prevention of

PE and, additionally, has decreased the demand for CT scan and perfusion scan diagnostic methods (16-20). The existence and application of smart systems to improve medical cares and reducing the number of DVT and PE cases seem to be essential considering the importance of the case and the issue of medical and diagnostic errors. As a correct prediction of a patient's condition as well a timely and precise diagnosis are of great importance, models with a minimum of errors and maximum of certainty must be employed. The purpose of this study is to predict the risk level of pulmonary embolism and deep vein thrombosis through artificial neural network.

2. 2. MATERIALS AND METHODS

2.1. The study population

This study is a scientific modeling and the population under investigation is patients suffering from PE and DVT who were hospitalized in 3 educational hospitals affiliated with Kerman University of Medical Sciences, located in the southeastern Iran, in a two-year period from late-August 2013 to mid-September 2015.

2.2. Sampling method and sample measuring

Considering the general rule of multivariate testing (21), 7 cases were assigned per risk factor and, hence, for this volume of samples, a number of 430 cases in 3 educational hospitals were investigated and after the omission of incomplete cases, a number of 294 complete cases were eventually selected for the present study with their perfusion scan results determined.

2.3. Method of data collection

A checklist of PE and DVT risk factors were initially was prepared based on the existent medical instructions and guidelines in the world (22) and subsequently, presented to a panel of experts including 1 pulmonologist, 2 hematologists and oncologists, and advising and supervising professors in order to investigate and prioritize the risk factors. The checklist was eventually refined based on the consults of the panel.

A number of risk factors were omitted from the list prior to the counsel of the specialist due to a lack of information and history in medical files. A number of other risk factors were merged together due to the similarities. Explanations on risk factors are presented below:

- Varicose veins (this factor was merged with "Other risk factors" in group 1).
- History of unexplained stillbirth infant, recurrent spontaneous abortion more than 3 times (this factor was omitted due to the lack of history in medical records).
- Obesity BMI > 40 and BMI > 50 (these factors were merged with "Obesity (BMI > 30)" in group 1 with the advice of the specialist)
- Laparoscopic surgery > 60 minutes and arthroscopic surgery > 60 minutes (these factors were merged with "Major surgery > 60 minutes" in the same group).
- Hematocrit factors such as V Leiden, Prothrombin 20210A, etc. (they were not found in medical records due to their rarity and costliness and thus omitted with the advice of the hematologist and oncologist).
- Elective major lower extremity arthroplasty (was merged with "Major surgery lasting over 3 hours").

Due to the high frequency of various surgeries in medical records and in order to categorize these surgeries based on the risk factors checklist, the advice of several specialists was sought and the categorization of surgeries was determined. In addition to the risk factors mentioned in the checklist, other variables such as the result of the treatment (recovery or death) were recorded alongside with the code of the medical record. The criterion for the omission of any case was its incompleteness where the incomplete cases were replaced with complete ones based on sampling methods. Prior to the determination of all risk factors pertaining to every patient, the index of Total Risk Factor Score (TRFS) (22) were computed for each patient according to which patients were categorized under the four groups of "Low Risk", "Moderate Risk", "High Risk", and "Highest Risk".

2.4. Method of data analysis

The software "MATLAB" (version 2014) was utilized to analyze the data and design the artificial neural network. In the stage of data preparation in order to design the ANN and prevent the error of over-processing, from the total number of 294 samples, 80 percent (235 samples) were randomly assigned to training set and the remained 20 percent (59 samples) were assigned to test set. In the present study, different models of Feed-forward back-propagation neural network were compared and contrasted with models of Elman back-propagation neural network in order to train and test the data as well as obtaining an optimized model. The learning is supervised and the training the networks is of error back-propagation kind. The structure of the network consists of 31 neurons in the input layer, 1 neuron in the output layer and different numbers of 5, 10, 15 and 20 neurons in the hidden layer with transfer functions of Tangent Sigmoid and Logarithm Sigmoid, and 8 training algorithms of BR, CGB, GDA, GDX, LM, OSS, RP, and SGC. After training each neural network model, the performance of each was studied in the experimental group and their efficiency was evaluated using MAPE (Mean Absolute Percent Error) and the errors in categorizing patients based on the risk level of the incidence of PE and DVT were detected.

3. RESULTS

The highest age frequency of the studied population was the age range of 41 to 60 years old. 44.21 percent of the population was male and the other 55.78 percent was female. The frequency distribution and frequency percentage of risk factors have been illustrated in 5 categories in Table 1 in order of their risk score. Among the risk factors (22), the highest frequent ones in the first category were "medical patient currently at bed rest", "age 41-60 years", "swollen legs (current)", and "history of prior major surgery, respectively. The least frequent factors in the same group were "obesity (BMI>30)" and "acute myocardial infarction (<1 month)". There were only 2 risk factors in the second category which was only related to female cases. The most and least frequent factors in the third category were "age 61-74 years" and "previous malignancy", respectively. In the fourth category, the most frequent factor was "history of SVT, DVT/PE" and the least frequent one was "family history of DVT/PE". And eventually in the fifth group, the factor of "multiple trauma (<1 month)" was the most and "acute spinal cord injury (<1 month)" was the least frequent factor.

	Feature	Number	% of Number
Each Risk Factor Represents 1 Point			
1	Age 41-60 years	91	30.95
2	Minor surgery planned	36	12.24
3	History of prior major surgery	83	28.23
4	History of inflammatory bowel disease	17	5.78
5	Swollen legs (current)	85	28.91
6	Obesity (BMI >30)	7	2.38
7	Acute myocardial infarction (< 1 month)	7	2.38
8	Congestive heart failure (< 1 month)	16	5.44
9	Sepsis (< 1 month)	9	3.06
10	Serious lung disease incl. pneumonia (< 1 month)	13	4.42
11	Abnormal pulmonary function (COPD)	29	9.86
12	Medical patient currently at bed rest	294	100
13	Leg plaster cast or brace	19	6.46
14	Other risk factors	9	4.42
Each Risk Factor Represents 1 Point (for women only)			
15	Oral contraceptives or hormone replacement therapy	12	4.08
16	Pregnancy or postpartum (<1 month)	26	8.84
Each Risk Factor Represents 2 Point			
17	Age 61-74 years	51	17.34
18	Major surgery (> 60 minutes)	33	11.22
19	Previous malignancy	2	0.68
20	Central venous access	6	2.04
Each Risk Factor Represents 3 Point			
21	Age 75 years or more	47	15.98
22	Major surgery lasting 2-3 hours	18	6.12
23	History of SVT, DVT/PE	106	36.05
24	Family history of DVT/PE	3	1.02
25	Present cancer or chemotherapy	32	10.88
26	Heparin-induced thrombocytopenia (HIT)	4	1.36
Each Risk Factor Represents 5 Point			
27	Hip, pelvis or leg fracture (< 1 month)	21	7.14
28	Stroke (< 1 month)	7	2.38
29	Multiple trauma (< 1 month)	22	7.48
30	Acute spinal cord injury (paralysis)(< 1 month)	6	2.04
31	Major surgery lasting over 3 hours	7	2.38

Table 1. Feature/percentage of risk factors (in five categories)

Risk assessment score for venous thromboembolism is based on the number of patient risk factors that have been found from epidemiological studies (22). The frequency distribution of the incidence of PE and DVT in patients using the TRFS index is shown in Table 2. According to the results of this table, from the 294 cases under study, the lowest number of 5 cases is at the risk level of "low risk", while 190 cases are at the risk level of "highest risk".

% of Number	Number	Risk Level
1.7	5	Low Risk
12.58	37	Moderate Risk
21.08	62	High Risk
64.62	190	Highest Risk

Table 2. The probability of PE and DVT in patients based on the TRFS index

3.1. Analysis and selection of the best artificial neural network model

The efficiency of a total number of 150 ANN models of two structures, namely Feed-Forward Back Propagation and Elman Back Propagation was evaluated using MAPE. The minimum MAPE in the Feed-Forward Back Propagation neural network pertained to BR and CGB algorithms with the rate of 3.38 and with a transfer function of tangent sigmoid and a number of 5 and 10 neurons respectively in their hidden layer. However, at the time of testing the networks against samples, the classification errors of 6 was reached. Concerning the neural network with the BR algorithm, a transfer function of tangent sigmoid with 20 neurons in its hidden layer, a MAPE rate of 4.25, and 7 errors in classification was reached. The best Feed-Forward Back Propagation neural model with a MAPE of 4.35 was the LM training algorithm, with a transfer function of tangent sigmoid including 10 neurons in its hidden layer and the lowest classification errors of 4.

The minimum MAPE in Elman Back Propagation neural network pertained to LM algorithm with the rate of 3.75, transfer function of logarithm sigmoid and a number of 20 neurons, yet 6 classification errors were noticed while being tested. In case of the neural network with the RB algorithm, tangent sigmoid transfer function with the respective 15 and 20 number of neurons in their hidden layer, a MAPE equal to 4.27 and classification errors of 6 were reached. The best Elman Back Propagation neural network with a MAPE rate of 4.43 was associated with the LM training algorithm and the transfer function of tangent sigmoid with 20 neurons in the hidden layer which accomplished the lowest number errors, 4, in the classification process. The results obtained from comparing the best model of Feed-Forward Back Propagation and the best model of Elman Back Propagation ANNs are shown in Table 3.

Model Number	Network type	Learning Method	Transfer Function	Number of neurons in hidden layer	MAPE (%)	Incorrectly Classified Instances
1	Feed-forward backprop	Train LM	TanSig	10	4.35	4
2	Elman backprop	Train LM	TanSig	20	4.43	4

Table 3. Comparison and contrast between the best structures of Feed-Forward Back Propagation and Elman Back Propagation artificial neural networks based on MAPE and the fewest classification errors

According to the obtained results, Feed-Forward Back Propagation ANN was selected as the optimized neural network with the structure of NN (31-10-1), MAPE=4.35, LM training algorithm, transfer function of tangent sigmoid, and the correlation coefficient of 97 percent comparing to the best model of Elman Back Propagation neural network with the structure of NN (31-20-1), MAPE=4.43, LM training algorithm, transfer function of tangent sigmoid, and the correlation coefficient of 95 percent. The reasons of this selection were its best performance, highest correlation coefficient in training stage, lowest number of neurons in the hidden layer, and fewest errors in training stage. The diagram of the course of the errors for training input in the optimized artificial

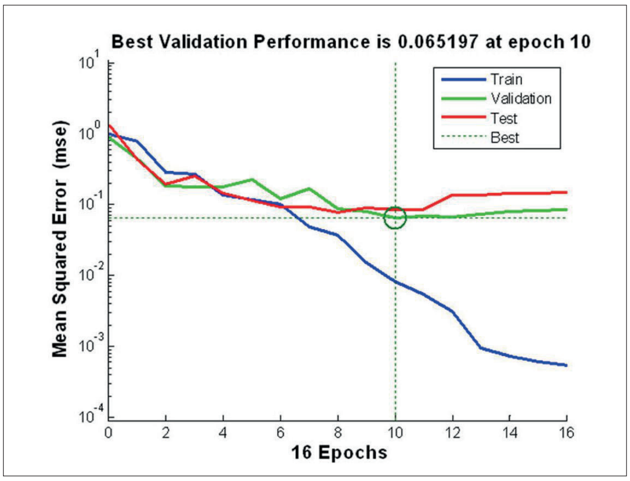

Fig. 1 Best Mean Squared Error (MSE) at 16 epochs

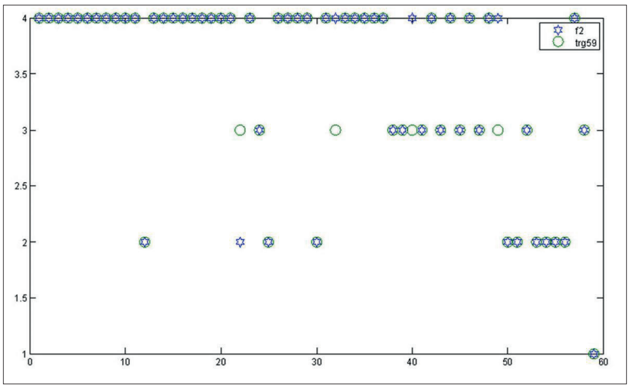

Fig. 2 The comparison between the predictions of risk level in predisposed patients to VTE with the real results in the optimized artificial neural network model

neural network model is illustrated in Figure 1.

3.2 Prediction of risk level in predisposed patients to VTE

In order to predict the risk level in predisposed patients to VTE, the output of the test set in the optimized artificial neural network model was compared to the real results in Figure 2. The real results and prediction results were marked with circle and star signed respectively, and the existing incongruity indicates the presence of errors. Note that the four risk levels of "low risk", "moderate risk", high risk", and "highest risk" were enumerated from 1 to 4 respectively.

As illustrated in Figure 2, a number of 4 errors can be noticed in the prediction of "high risk" patients. In other words, 1 case of "high risk" patients is categorized under the level of "moderate risk" and another 3 are categorized under the level of "highest risk". Hence, an accuracy rate of 93.23 was achieved in this study considering these results.

3.3 Analysis of statistical results

In order to calculate the relation between VTE risk level and mortality in patients, Chi-square Test was employed in this study and a P Value of 0 was achieved. Considering the results of this test which can be found in Table 4, it can be clearly noticed that there is a significant relation between VTE risk level and mortality in patients.

3.4 Comparison of the study and Perfusion Scan results

Perfusion scan is a diagnostic method conducted to determine the risk level of predisposed patients to VTE. To compare the results obtained from this study to those from Perfusion Scan method, Chi-square Test was applied. The results of the test indicate that the incidence risk of VTE based on the results obtained from Perfusion Scan – 104 low risk patients (4.8 percent), 64 moderate risk (23.8 percent), and 127 high risk patients (86.6 percent)- were in accordance with the results of this study (Table 5).

Total	Dead		Risk Level
	Yes	No	
5	5	0	Low Risk
37	36	1	Moderate Risk
62	60	2	High Risk
190	147	43	Highest Risk
294	248	46	Total

Table 4 Frequency distribution of VTE risk level and mortality in patients

The Study Results			Perfusion Scan Method
High Risk (%)	Moderate Risk (%)	Low Risk (%)	
0	0	4.8	Low Risk (%)
13.4	23.8	64.8	Moderate Risk (%)
86.6	75.8	30.5	High Risk (%)

Table 5 Comparison of the results of the study with the results from Perfusion Scan

4. DISCUSSION

For the first time in Iran, the present study has proposed a system in order to determine the risk level of the incidence of pulmonary embolism and deep vein thrombosis using an artificial neural network. The proposed model is capable of predicting the condition of patients based on categorizing them into 4 groups, namely: "low risk", "moderate risk", "high risk", and "highest risk". The risk factors checklist prepared for PE and DVT has a number of strengths including being developed in a panel of experts, being simple and containing the point of view of different specialists based on whose opinions a study has been conducted on the prediction of PE and DVT incidence (23). The data for this study has been gathered from the medical records present in 3 educational hospitals and since every of these hospitals provide different medical services, therefore, data collection and classification of patients based on checklist of risk factors turned out to be more variety and comprehensive.

Two types of artificial neural networks, namely Feed-Forward Back Propagation and Elman Back Propagation, were compared in this study in order to train and test the data and achieve the optimized model. It is worth mentioning that 4 patients were not correctly classified in both models, however Feed-Forward Back Propagation Network has a higher convergence speed and requires fewer neurons in its hidden layer. Based on the results, a prediction accuracy and correct index of 93.23 percent was achieved through the optimized neural network. After the comparison of the results gained from this study with the results from perfusion scan method, it was learned that 4.8 percent of low risk patients, 23.8 percent of moderate risk patients, and 86.6 percent of high risk patients were diagnosed correctly. Thus, this CDSS designed based on valid medical advice is capable of diagnosing 86.6 percent of high risk patients.

This result is of great significance as the patients who are in need of prompt diagnostic and treatment procedures can be detected as quick and accurate as possible. Moreover, the probable side effects and damages caused by Perfusion Scan Diagnostic Method can be avoided for those patients who do not require such procedures. Furthermore, it is possible to develop a more comprehensive ANN based on more data from hospitals in the future to assist patients. The results of this study indicate the ability of the optimized neural network in risk level prediction of predisposed patients to PE, at the same time, in accordance with other studies conducted in the world.

In a study conducted by Patil et al. despite having a larger sample size and higher number of variables comparing to this study, an optimized model with 10 neurons in its hidden layer was developed (24). In another study carried out by Falsetti et al. the clinical prediction of PE, akin to this study, was based on Geneva and Wells risk factors. The sample size of Falsetti study was larger than this study, however, the number of their risk factors were lower. The cause of the reduction of neurons in the hidden layer can be well-conducted risk factor selection and efficient training of the neural network (18). Rucco et al. used a combined ANN, more advanced methods, and a larger sample size in their study and achieved an accuracy index of 94 percent in prediction (19). Whereas, in this study two different types of neural networks and a higher number of risk factors were utilized.

5. CONCLUSIONS

Considering the application of Clinical Decision Support Systems (CDSS) in healthcare as well as diagnostic and treatment procedures, the results of the present study are of importance and efficiency. Additionally, healthcare specialists and politicians in the field of healthcare will be assisted, through the implementation of the proposed model, to diagnose patients who are really in need of treatment procedures promptly and prevent the number of mortalities. According to a report by Kucher et al., if CDSSs are installed and utilized in hospitals, the number of PE and thrombosis cases will decrease by approximately 41 percent (25). It is expected that this designed system alongside with pulmonologists, hematologist, orthopedists, surgeons, etc. can reduce the risk of the incidence of PE and DVT in predisposed patients to this condition and the number of effective diagnostic costs.

Limitations

This study faced some difficulties and limitations such as:

The system for recording the patients' medical information was paper-based.

The handwriting of some medical staff and physicians was illegible.

Studying and investigating the medical records was time consuming and required sufficient expertise and attention.

Due to the high number of risk factors and medical records, the data was scattered in medical records.

In case of patients whom have undergone surgeries, there was no mention of the duration of the surgery in the patients' medical records. To tackle this issue, a list of all performed surgeries was initially prepared by the researcher and, subsequently, prior to making the required arrangements with surgeons in different fields of specialty (orthopedic, neurosurgery, urology, ophthalmology, cardiovascular, gynecology, and general), the duration of each surgery was determined and recorded.

A higher number of variables had to be included in this study, however, due to the absence of medical history and incidence of complications in the database, a number of variables were omitted to reduce errors.

Recommendations: A number of suggestions can be made based on this study including: Utilizing higher sample size in future studies, Optimizing the structure of artificial neural networks through other intelligent methods such as genetic algorithm and fuzzy algorithms., Clinical trial of the system designed as research projects, Gradually extinguishing the paper-based system for recording medical information and developing an electronic medical record (EMR) to facilitate faster and easier searches and more comprehensive databases.

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Ethical considerations: This study was passed in the ethical committee of Kerman University of Medical Sciences with the code number 5620. Other ethical elements that were fully observed include the accuracy and correctness of data gathering as well as data analysis and the confidentiality of the patients' information.

• Conflict of interest: none declared.

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