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Using Machine Learning Methods for Predicting Inhospital Mortality in Patients Undergoing Open Repair of Abdominal Aortic Aneurysm

Ana Monsalve-Torra^a, Daniel Ruiz-Fernandez^{b,*}, Oscar Marin-Alonso^a, Antonio Soriano-Payá^b, Jaime Camacho-Mackenzie^c, Marisol Carreño-Jaimes^c

^aBio-inspired Engineering and Health Computing Research Group. IBIS. University of Alicante, Spain ^bDepartment of Computer Technology of the University of Alicante, Spain ^cDepartamento de cirugía cardiovascular - Fundación Cardioinfantil- Instituto de Cardiología. Bogotá-Colombia

Abstract

An abdominal aortic aneurysm is an abnormal dilatation of the aortic vessel at abdominal level. This disease presents high rate of mortality and complications causing a decrease in the quality of life and increasing the cost of treatment. To estimate the mortality risk of patients undergoing surgery is complex due to the variables associated. The use of clinical decision support systems based on machine learning could help medical staff to improve the results of surgery and get a better understanding of the disease. In this work, the authors present a predictive system of inhospital mortality in patients who were undergoing to open repair of abdominal aortic aneurysm. Different methods as multilayer perceptron, radial basis function and Bayesian networks are used. Results are measured in terms of accuracy, sensitivity and specificity of the classifiers, achieving an accuracy higher than 95%. The developing of a system based on the algorithms tested can be useful for medical staff in order to make a better planning of care and reducing undesirable surgery results and the cost of the post-surgical treatments.

Keywords:

Machine learning, mortality prediction, abdominal aortic aneurysm, clinical decision support system, data analysis.

1. Introduction

An aneurysm is a progressive and localized dilation (a diameter increase over 50% of normal size) that compromises the three layers of a vessel. This disease is most common in overaged people, males, smokers, and those with a family history of aneurysms. It is also the tenth leading cause of death in men aged over 60 and it is becoming more and more common in women [1, 2]. Aneurysms are classified according to shape (fusiform, sacular), size (macroaneurysm, microaneurysms), placement (central, peripheral, visceral and cerebral) and structure (true and false). The most common location is infrarenal with an incidence from 2% to 6% in people over 60 years [3]. An abdominal aortic aneurysm (AAA) (Figure 1) is a focal dilatation at some point of the abdominal section of the aorta [4]. Considering that the normal diameter is from 1.5 to 2.4 cm, aneurysms can be diagnosed when the transverse diameter of the aorta goes up to 3cm or greater [5]. Without any treatment the AAA leans to grow until rupture. For its treatment (reparation) there are two main techniques: open repair, which is an invasive surgical procedure; and the endovascular aneurysm repair, which is transcatheter procedure where a stent graft is inserted using a catheter in order to exclude the aneurysm from the blood circulation [4].

The AAA prevalence in the general population is between 1-1.5% [6] becoming a common disorder in elderly patients [3]. Regarding AAA diagnosed women, available literature shows a prevalence rate between

^{*}Corresponding author at: Department of Computer Technology. University of Alicante, Ctra. San Vicente del Raspeig s/n, San Vicente del Raspeig (Alicante) - 03690, SPAIN, Tel +34 965903400 x 3331 *Email address:* druiz@dtic.ua.es (Daniel Ruiz-Fernandez)



Figure 1: Abdominal aortic with aneurysm (repaired)

0.7% to 1.5%, which is significantly lower than the 6% to 8% prevalence found in males [7]. Mortality rates are remarkable in patients suffering from AAA. Studies show that AAA is responsible for 1-2% of death in men [8]. However, reports based on over the past two decades suggest that the mortality associated with AAA has declined. For instance, in United States mortality in 1999 went up to 10,464 cases and, later 6,289 cases were reported in 2010 [9]. In Spain, between 2002 and 2004, 2,614 patients over 40 years (2,343 men and 271 women) died due to AAA [10]. In 2011 there was a reduction of that number being 1,866 (1,582 men and 327 women) [11]. Overall inhospital mortality is between 4 - 7% [9]; in the United Kingdom, in a multicentre study from February to May 1999 the overall inhospital mortal

tality rate was 7.3% [12]. In Colombia, a study carried out between 1999 and 2014 (Fundación Cardioinfantil) in patients with AAA underwent surgery shown a mortality between 1.3% - 28.6% [13].

To study and analyse the tend of inhospital mortality, the medical and clinical staff use mechanisms such as epidemiological studies and mortality review committees, among others. The addition of other instruments as machine learning methods could improve the prediction of operative mortality, reducing the risks of making incorrect decisions, and hastening processes of diagnostic data analysis. The objective of our work is to develop a clinical decision support system testing different machine learning algorithms based on artificial intelligence to predict inhospital mortality of patients who were undergoing open repair of AAA. We used artificial neural networks as multilayer perceptron or radial basis functions networks, and a Bayes-based method.

2. Background

The use of artificial neural networks (ANN) and bayesian networks (BN) as tools to support clinical decision making is in continuous growth. We can find multiple examples of that use. In neurology for predicting the mortality of haemorrhagic and ischemic patients within the first 10 days after a stroke [14]. In the prediction of symptomatic cerebral vasospasm after aneurysmal subarachnoid haemorrhage; the ANN offers the advantage of estimating non-linear relationships that are dropped by logistic regression models [15]. Predicting long-term outcome after traumatic brain injury using repeated measurements of Glasgow Coma Scale [16]. ANNs have been used also in works related to respiratory system, for predicting mortality after lung transplantation [17] and early prediction of the high workload for analysing the possible cardiac failures [18]. Also in other areas as oncology, prediction 5-year mortality after surgery for hepatocellular carcinoma and performance comparison with logistic regression models [19]. Predicting whether patients have cancer or not [20], the mortality after radical cystectomy as

definitive treatment [21] and the survival following liver resection for colorectal cancer metastases [22]. In vascular surgery, for the prediction of inhospital mortality after ruptured abdominal aortic aneurysm repair [23]. In this work cases studied are just from extreme situations after a rupture; our work includes surgery previous to a future rupture. Also to predict postoperative morbidity of endovascular aneurysm repair [24]. Regarding, BN, they have been used to predict unstable angina [25] and for the prediction of hospital-acquired pressure ulcers [26].

Focusing in hospital mortality prediction associated with AAA, there is little research published about the topic. In [27] the purpose of the study was to compare the results of the use of multiple regression modelling techniques and ANN, for predicting AAA in-hospital mortality. Later, these results were contrasted with clinicians' estimations prognosis. Authors measured the results using Receiver Operating characteristic Curve (ROC) with the following values: multiple regression 0.869, ANN 0.842 and clinicians 0.816. In this paper, multiple regression offered the best results.

The use of ANN provides features such as adaptability, fault tolerance, parallel processing, robustness, nonlinearity and classifying when there is noise within de input data [28]. BN models present the ability to handle uncertainty and missing data allowing high predictive accuracy and the ability to represent the complex causal relationships of multiples variables on surgical treatment [29]. For these reasons we have chosen to test the ANN and BN in our work.

3. Methods

3.1. Data set

The data used in this study comes from patients who underwent open repair of AAA from 2002 to 2012 at the Fundación Cardioinfantil - Instituto de Cardiología (Colombia). The database was designed following the practice guidelines for care of patients suffering an AAA of the Society for Vascular Surgery [30]. For the present analysis, we include data of 57 attributes from 310 cases. Out of this set of patients, 92.6% survived and 7.42% died after surgery. The attributes are grouped into four clusters: patient's basic data, clinical history, surgical data and postsurgical data. They represent information such as age, gender, weight, high blood pressure, diabetes, the length of stay, diagnosis, medication prescripted, complications, etc. Appendix A shows a list of the attributes and their possible values.

Attributes were pre-processed attending to its nature and the range of values they could have. For instance, attributes related to some conditions that the patients may have suffered like heart failure, acute myocardial infarction, stroke, chronic obstructive pulmonary disease or kidney disease are binary, classified using 1 if the condition is present in the clinical history or 0 otherwise. The same for other attributes related to habits like smoking. In other cases, with non binary attributes, the possible options were codified associating a numeric value to each case, e.g.: length of stay at intensive care unit (normal=1, long=2), postoperative length stay (normal=1, long =2).

3.2. Algorithms tested

Within machine learning, we can find effective methods for knowledge discovering in a database, being able as well to integrate data from different sources. From the machine learning algorithms used for classification and prediction, we have selected the following: multilayer perceptron (MLP) because of its easy implementation and the ability to generalize, among others; radial basis function networks (RBF), which have advantages such as strong tolerance to input noise, high accuracy and fast convergence. Finally, bayesian networks present abilities as easy understanding and incomplete data sets handling.

3.2.1. Multilayer perceptron

MLP is one of the supervised ANNs most frequently used in clinical decision support systems. A MLP is based in a groups of units, called perceptrons, divided in different layers. The basic concept of a single perceptron was introduced by Rosenblatt [31]. A MLP can

consist of three or more layers: an input layer that receives external inputs, one or more hidden layers and an output layer.

Currently, the backpropagation architecture is the most popular and easy learning model for multi-layered networks. The backpropagation name comes from the way the error is backpropagated through the neural network, in other words, the error is propagated backward from the output layer [32]. This allows to update values of weighted connections of the neurons placed in the hidden layers during training stage. It has a generalization ability that allows to provide satisfactory outputs based on inputs that the system has never seen in the training phase. The expression for standard backpropagation is [33]

$$\Delta w_{ij}(t) = \alpha \delta_i o_i \tag{1}$$

Where $\Delta w_{ij}(t)$ is a change in the weight between neurons *i* and *j* during the iteration (*t*), α is a learning rate, δ_j is an error associated to neuron *j*, and o_i is the output of the preceding neuron *i*. A non-linear function called "activation function" is applied to the exit of the output layer in order to activate the corresponding neuron. A sigmoid function is commonly used for that purpose, as it is the case of our work. Since MLP follows a supervised learning process, during training stage we know the expected output for a certain input. A quadratic function is applied to the difference between the actual output value and the expected one for each output unit.

The MLP implemented in this work has the following architecture:

Layer 1: it is the input layer. It has as many nodes as clinical attributes are in the dataset in order to predict the inhospital mortality of patients who underwent open repair of AAA.

Layer 2: the hidden layers. To decide the number of neurons in the hidden layers is a key part of determining the overall MLP. Both, the number of hidden layers and the number of neurons in each of these layers, it must be carefully considered. Using too few neurons will result in under-fitting, meanwhile, too many neurons may result in over-fitting [34]. The number of hidden layer and neurons will depend on each problem. In our case we have used 3 hidden layers with 4 neurons in each. The values for other parameters are: learning rate = 0.5and epoch (training iterations) = 500. These parameters were empirically established and they showed the best results for the prediction.

Layer 3: output layer. It has one neuron, associated to the possible output values. Since we are predicting mortality of patients, these values will be: death (1) or alive (0).

3.2.2. Radial basis function networks

They were introduced by Broomhead and Lowe [35]. They consist of three layers: an input layer, a hidden layer and an output layer (Figure 2). The main processing and classifying task within these networks is carried out in the hidden layer by means of the nodes placed in it. These nodes (or units) implement a radial basis function each one. Most commonly, these functions have the shape of a Gaussian function, which makes them perfect for being used as non-linear transfer functions. The input for those functions consists of the patient-associated data (basic, surgical, clinical, post-surgical, etc.). The transfer functions centre position and width are parameterized in order to build suitable solution spaces for the classifying problem faced by aggregation of each unit's RBF. In our design, hidden layer consists of 3 nodes. Finally, the processing element in the output unit estimates its output as a linear combination of outputs from the hidden layer [36].

In our case we have used a hybrid learning process for the RBF. This method consists of two stages. In a first unsupervised stage the centres and the amplitudes of the neurons in the hidden layer are determined. Then, in a second supervised stage the weights and thresholds of the output layer are determined.

3.2.3. Bayesian networks

BN can be used as classification algorithms in which the predictive and descriptive class is based on the



Figure 2: Common architecture of radial basis function network

Bayes theorem [37]. BN are a widely used paradigm in Artificial Intelligence because they have the capability to working with incomplete information, a flexible capacity for specifying dependence and independence between variables and, finally, their structure tend to follow the logic inherent in a decision task [38]. They are a model that consists in an acyclic graphic (Figure 3) in which each node represents a variable and each arc denotes a conditional dependence and the probability distribution [39]. According to the task of sorting, the bayesian classifiers can be: Tree Augmented Bayes Network (TAN), Augmented Bayes Network (BAN) and Naive Bayes classifier (NB). TAN is based on the structure of the Naive Bayes but the learning process allows connection between nodes in a tree. It also assumes that a set of attributes can be causally dependent [40]. BAN algorithm produces the maximum likelihood structure given the constraint that each node can have at most one dependent node in addition to the root node [41]. NB assumes that the attributes values are conditionally independent. After several test we have chosen NB as classifier and the algorithm K2 (which uses a hill climbing algorithm restricted by an order in the variables [42]) as search algorithm.



Figure 3: A section of our bayes network graph

4. Experiments and Results

4.1. Experiments

Several tests have been carried out with MLP, RBF and bayesian networks. The implementation, learning and testing steps were performed using Waikato Environment for Knowledge Analysis (WEKA), developed at the University of Waikato (New Zealand) under GPL license [43].

At the training stage we used cross-validation technique to asses the generalization ability of each algorithm used. Available data was randomly splitted in 10 equally-size subsets or folds. Then we used each single subset for validation and the remain ones for training along 10 iterations.

To assess the performance of the algorithms, we had the following measures: accuracy, sensitivity and specificity. The sensitivity and specificity are measures of probability of the performance of a binary classification test. In our case, positive results are associated to patients predicted to die after surgery (measured using sensitivity rate, also called true positives rate) and negative results to patients who are predicted to live (measured using specificity rate, also called true negatives rate). In this point it is important to remember that the objective of this work is associated to the prediction of inhospital mortality in order to make a better plan of care and avoid high risk procedures. We can see in table 1 the expressions for each of metrics used.

Table 1: Performance assessment test.	
	Expression
Sensitivity	TP/(TP+FN)
Specificity	TN/(FP+TN)
Accuracy	(TP+TN)/(TP+FP+FN+TN)

Where TP = true positive, TN = true negative, FP = false positive and FN = false negative [44].

4.2. Results

We have developed two type of experiments. Firstly, using all variables and later on, carrying out a feature se-

lection process. It is worth to mention that the accuracy of all tested algorithms (in all experiments) was higher than 91%, which means that in overall the performance of the algorithms were good, but each had remarkable differences in the sensitivity and the specificity.

Regarding with the first group of experiments (with all the variables), we can see in table 2, that the sensitivity (the probability of correctly predicting that a patient will die after surgery due to AAA) for BN is 73% and specificity (the probability of correctly predicting that a patient will survive) goes up to 92.6%. For RBF the sensitivity is 52.1%, whereas that the specificity is 96.1%. For MLP the same measures are 65.2% and 97% respectively. Results obtained, especially, for these algorithms are not good enough to be considered for an aid decision system. Consequently, we continued with the second group of experiments.

Table 2: Metrics associated to mortality prediction of each classifier using all variables.

Algorithm	Sensitivity	Specificity	Accuracy
	(%)	(%)	(%)
MLP	65.2	97	95.1
RBF	52.1	96.1	92.9
BN	73	92.6	91.2

In the second stage, we applied a feature selection process. The aim of this features selection is to reduce the computational complexity, the overfitting and to improve the classifiers generalization [45], in order to obtain a better sensibility. We used as attribute evaluator the *TheBestfirst*, which searches the space of attribute subsets by greedy hillclimbing, augmented with a backtracking facility [43]. The selected attributes (9) are identified as (*) in the Appendix. In table 3, we can see the metrics assessed after features selection and we can observe an improvement specially for RBF and BN.

Although we obtained good results in sensitivity with the BN method, we tried to improve this measure combining the three methods used. We have applied a combination of the three algorithms with the following condition:

 Table 3: Metrics associated to mortality prediction of each classifier after feature selection process.

Algorithm	Sensitivity	Specificity	Accuracy
7 Hgoritinii	Sensitivity	Specificity	recuracy
	(%)	(%)	(%)
MLP	65.5	98.2	95.8
RBF	69.5	98.6	96.4
BN	86.8	96.8	96.1

mortality= if(MLP=1 or RBF=1 or BN=1;1;0)

A combination of algorithms improves the results for the prediction of mortality in the two stages (table 4), obtaining a growth in the sensitivity when all the variables are used and a slight increase (comparing with BN algorithm) with features selection. The specificity and the accuracy continue being significantly higher.

 Table 4: Metrics associated to mortality prediction of each classifier using a combination.

Stage	Sensitivity	Specificity	Accuracy
	(%)	(%)	(%)
All variables	82.6	95.1	94.1
Feature selection	87	96.1	95.4

5. Discussion

As it has been previously showed in the results section, multilayer perceptron and radial basis function networks present the highest global accuracies, when they are tested with all variables 95.1% and 92.9% respectively. However, they provided low sensitivity rates (65.2% - 52.2%), which is related to mortality prediction. We have done experiments using features selection with the objective of improving the sensitivity and the results were specially good for BN reaching a 86.8% in sensitivity; MLP and RBF had a sensitivity of 65.5% and 69.5% respectively. Finally, we have improved the sensitivity results combining the algorithms; a combination of the three classifiers tested gave an improvement of the sensibility (reaching a 82.6% with all the variables and 87% with features

selection), keeping the specificity and accuracy higher than 94% in both stages, with all variables and with features selection.

The unbalanced data is one of the problems we are facing when working with this medical dataset because 92.6% of data are from patients who survived to the surgery and 7.42% patients who died. This issue can affect the performance of the classifiers, such is the case of the multilayer perceptron and radial basis function networks.

The prediction of mortality after open repair surgery of abdominal aorta aneurysm represents a major challenge for the medical community overall. The development of a clinical decision support system based on the use of machine learning methods like those we have tested could enhance the prediction of inhospital mortality. Moreover, a clinical decision support system could be useful for physicians and medical staff assessing the impact of decisions related to interventions or treatments after, during and in the post-surgery stage prioritizing the prevention of mortality activities, to get a better a distribution of services and resources.

Finally, comparing our results with other studies, we can observe that, for the cited [27] the best results were obtained from multiple regression and ANN, whereas in our work, the best results were provided by Bayes network. This suggests that research in the use of machine learning methods can be enhanced in order to predict inhospital mortality in patients with AAA.

6. Conclusions

According to the obtained results, tested methods can be useful to help clinical staff to improve the results in AAA repair surgery taking a special care of those patients who have a high risk of mortality; additionally, this tool could increase the productivity of the processes in the mortality committees and the epidemiological analysis data and its understanding.

BN is the best algorithm in all tests presenting in the first group of tests (using all the variables) an accuracy 91.2%, a sensitivity of 73% and a specificity of 92.6%. When a features selection process is done, the results improve and BN reaches an accuracy of 96.1%, a sensitivity of 86.8% and a specificity of 96.8%.

In order to improve the sensitivity results we have combined the three algorithms tested and, thanks to this combination, we have obtained a higher sensitivity, reaching a 87% when features selection is used and keeping the specificity higher than 95%.

Appendix A. VARIABLES DATABASE

Patient's Basic Data	Values
Age group	1:[78 to 93], 2:[77 to 62]
	3:[61 to 42]
Gender	1 = male; 0 = female
Body mass index	1:[underweight],
	2:[underweight]
	3:[overweight],
	4:[moderately obese]
	5:[severely obese]
Clinical History	
Risk	0 = ruptured; $1 =$ elective
Elective*	0 = no; 1 = yes
New York Heart Association	
(NYHA) Functional	
Classification	[1,2,3,4]
ASA*	1:[normal healthy patient.],
	2:[patient with mild systemic
	disease.],
	3:[patient with severe systemic
	disease.],
	4:[patient with severe systemic
	disease that is a constant
	threat to life.],
	5:[moribund patient who is not
	expected to survive]
Hta (HBP)	0 = absence; 1 = present
Diabetes	0= absence;1= present
ICC (CHF)	0 = absence; 1 = present
ECV (stroke)	0:[ait],1:[absence],3:[stroke]

	Dyslipidemia	0 = absence; 1 = present
	Acute myocardial infarction	0 = absence; 1 = present
	Angina pectoris	0 = absence; 1 = present
	Angina pectoris kind	0:[without angina],
		1:[stable],
		2:[unstable angina]
	Chronic obstructive-	
	pulmonary disease	0 = no; 1 = yes
	Renal failure	0 = no; 1 = yes
	Vascular surgery*	0 = no; 1 = yes
	Not heart surgery	0 = no; 1 = yes
	Heart surgery	0 = no; 1 = yes
	Previous myocardial-	-
	revascularization	0 = no; 1 = yes
	Angioplasty	0 = no; 1 = yes
	Smoking	0 = no; 1 = yes
	Beta-blockers	0 = no; 1 = yes
	Steroids	0 = no; 1 = yes
	Surgical Data	Values
	Nitrates IV	0 = no:1 = ves
	Oral nitrates	0 = no:1 = ves
	Aspirin	0 = no; 1 = ves
	Anticoagulants	0 = no; 1 = ves
	IECA	0 = no; 1 = ves
	ARA II	0 = no; 1 = ves
	Diuretic	0 = no(1 = ves)
	Clopidogrel	0 = no; 1 = ves
	Hypolipemiants	0 = no; 1 = ves
	Previous ejection fraction	1.[20 to 50]
	Trevious ejection fraction	2:[51 to 55]
		$3 \cdot [56 \text{ to } 60] 4 \cdot [> 60]$
	Type of surgery	$1\cdot [n] anned 2\cdot [urgency]$
	Type of surgery	3:[emergency]
	Cod Vol aneurysm	1:[0 to 50] $2:[51 to 60]$
	Cou voi ancuryshi	$3 \cdot [61 \text{ to } 70]$ $4 \cdot [571]$
	Cod prosthesis	$1 \cdot [0 \text{ to } 16] 2 \cdot [18 \text{ to } 35]$
	Corps	1:[bifurcated] 2:[straight]
	Surgical approach	1.[outroparitonaal]
	Surgical approach	2:[transparitonaal]
	Cod total time surgery	2.[[1]allsperitoriear]
(Cou totai time surgery	$1.[00 \ 10 \ 120],$ $2.[121 \ to \ 180]$
		2:[121 to 180]
		$5:[181 \ 10 \ 240],$
	Cad alarra time	4 [> 241]
	Cod clamp time	1:[10 to 30],
		2:[31 to 50],
		3:[51 to /0], 4:[>/1]
	Cod bleeding*	1:[0 to 500],
		2:[501 to 1000],
		3:[1001 to 1500],
		4:[>1501]

Post-surgical Data	Values
Transfused	0 = no; 1 = yes
Surgery complication*	0 = no; 1 = yes
Cod postoperative-	
transfusions	1:[0], 2:[1 to 5],
	3:[6 to 10], 4:[>10]
Neurological complication	0 = no; 1 = yes
Renal complication*	0 = no; 1 = yes
Infectious complication	0 = no; 1 = yes
Pulmonary complication*	0 = no; 1 = yes
Vascular complication*	0 = no; 1 = yes
Cardiac complication	0 = no; 1 = yes
Other complication*	0 = no; 1 = yes
ICU length stay	1:[normal stay], 2:[long-stay]
In-hospital length stay	1:[normal stay], 2:[long-stay]
Postoperative length stay	1:[normal stay], 2:[long-stay]

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Highlights

Machine learning is used for predicting inhospital mortality in patients with AAA.

The methods tested provided an accuracy higher than 95%.

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