Artificial Neural Networks Prognostic Evaluation of Post-Surgery Complications in Patients Underwent To Coronary Artery Bypass Graft Surgery

Cesar Souza, Ednaldo Pizzolato,
Renata Mendes, Audrey Borghi-Silva
Departamento de Computação, Departamento de Fisioterapia
Universidade Federal de São Carlos
São Carlos, Brazil
cesarsouza@gmail.com; ednaldo@dc.ufscar.br;
mendesrg@hotmail.com; audrey@ufscar.br

Maurício Machado, Paulo Correa
Hospital de Base de São José do Rio Preto
Faculdade de Medicina de São José do Rio Preto
São José do Rio Preto, Brazil
maunmac@gmail.com, paulocorre@gmail.com

Abstract— **In this paper we explore the applications of artificial neural networks in the field of heart surgery, more specifically in the prognostic evaluation of post-surgery complications, such as death, reintubation, prolonged mechanical ventilation and the need for extracorporeal circulation in patients who underwent coronary artery bypass graft surgery. Predictive variables were limited to information available before the procedure, and outcome variables were represented only by events that occurred postoperatively. We also employed the principal component analysis technique to further reduce the complexity of our input data set in an attempt to improve artificial neural network efficiency and reliability.**

Keywords: Artificial Intelligence, Feedforward Neural Networks, Cardiovascular System, Coronary Artery Bypass Graft Surgery.

I. INTRODUCTION

Artificial neural networks have been successfully used in various areas of the human knowledge due to their solid theoretical foundation, robustness and ability to produce better results than other techniques for particular problems [1]. In some cases, the use of neural networks can be justified simply by the difficulty of finding an algorithm solution or when a direct solution would be too complex.

One of the areas the researchers have demonstrated interest is the area of health, as there is a great chance of saving human lives by predicting diseases or deaths. It is also possible to plan surgeries according to predicted hospitalization times.

Neural networks have been applied to clinical diagnosis [2] or to analysis and interpretation of images and signals with encouraging results [3][4]. In the specific area of prediction of the clinical outcome, there are many works demonstrating the usefulness of neural networks in health. Fraser and colleagues [5], for example, investigated the viability of using a specific kind of neural networks (radial basis function) to the diagnosis of myocardial infarct. The research was conducted using data gathered from 500 patients and results have shown sensibility of over 85%. Many other works have confirmed neural network viability in computer aided diagnostic systems: in the prediction of renal graft acceptability in renal transplants [6], in the diagnostic of rejection [7], in the selection of variables for prediction of chronic rejection [8], in the determination of cytomegalovirus in receptors [9], in immunosuppressive dosage [10], among others.

In this paper, we explore the use of feedforward multi-layer perceptron artificial neural networks in the prognosis of post-surgery complications, such as death (in 30 days), prolonged mechanic ventilation, need for extracorporeal circulation and need of reintubation in patients that underwent to coronary artery bypass graft surgery (CABG). It is structured as follows: in section 2 we present the motivation of this study and its usefulness. In section 3 we describe the methods. In section 4, we present the results and discussions. Finally, in section 5, we present our conclusions.

II. MOTIVATION

Coronary artery disease (CAD) originates from the coronary arteries failure to supply the metabolic needs of the cardiac muscle. About 75% to 80% of patients with CAD show conventional or classic risk factors, represented by hypercholesterolemia, arterial hypertension, tobacco addiction, diabetes mellitus, advanced age, familial occurrence, among others [11][12].

Although many alternative treatments exist for treating CAD, such as the clinic treatment and the tranluminal coronary angioplasty, surgery remains the most common for more complex forms of coronary artery disease. It is also the most lasting [13]. The surgery procedure aims at alleviating the symptoms, protecting the myocardial ischemic, improvement of ventricular function, acute myocardial infarct prevention and overall patient recuperation – physically, psychologically and socially [14]. This option has been considered as a safe and well established procedure, providing an increase in both life expectancy and quality of life [15].

Additionally, the development of artificial circulatory and oxygenation systems, known as Extracorporeal Circulation (ECC), revolutionized the cardiac surgery, allowing the maintenance of vital functions in patients undergoing the surgery procedure. This said, the coronary artery bypass graft surgery (CABG) combined with ECC is

978-0-7695-3926-3/09 $26.00 © 2009 IEEE
DOI 10.1109/ICMLA.2009.116

considered a "Gold Standard" procedure due to its excellent results and reproducibility in many centers, showing great results in up to 15 years of follow up [16]. However, besides the recognized great importance of the ECC in the CABG, the use of such technique is known to cause serious damage of systemic order [17].

Many complications have been remarked in literature about patients that underwent the cardiac surgery (CS). Those can develop a systemic inflammatory response syndrome due to surgery trauma, blood contact with non-endotelized surfaces of the extra-corporeal circuit and by the called post-EEC reperfusion injuries [17][16]. The development of humoral and cellular response occurs with non-infectious fever, leukocytosis, increase of capillary permeability, interstitial liquid accumulation, coagulation alterations and organ dysfunctions (mainly lung and heart) [18]. In addition to ECC, the intubation time and the use of artificial ventilation systems associated with esternotomy incision have been causing profound alterations to the patients' ventilatory pattern, leading to greater incidence of pulmonary complications and greater hospitalization times. They have also increased the mortality risk [19].

Thus, the prognostic of possible surgery complications during or after surgery is of great value in CABG. As its determination depends upon numerous abnormalities, indentified in one or more variables, multivariate classification patterns represent the most comprehensive and precise form of classification. In this context, the linear discriminant analysis, the multilinear regression and the logistic regression have been largely used in the cause-effect evaluation in the prognostic studies of many diseases [20]. However, a great part of problems in medicine, related to evolutionary group classification, cannot be adequately evaluated by linear separation methods. Thus, there is enough justification for the exploration of the applicability of artificial neural networks to the prognostic evaluation of possible surgery complications.

III. METHODS

Through a partnership with researchers from the São José do Rio Preto Hospital – Brazil (Hospital de Base de São José do Rio Preto), it was possible to gather a detailed data set of 848 patients who underwent CABG surgery, with a 30 day post-surgery follow-up for the variable "death" (Table 1). In order to test the generated data, we divided our patient data set (848 entries) into two disjunctive sets: the training set, containing 635 entries registered until 2007; and a testing set, containing 213 entries gathered between 2007 and 2008.

All input data (descriptors) have been analyzed, as shown in table I. We should point out that some of the values are boolean (true or false) and do not fit a normal distribution. The last four values in the table are the outputs of the neural networks. All others are input data.

In a first and classical approach, we have used the classical Multi-Layer Perceptron (MLP) model trained by the error backpropagation algorithm [21] to create artificial neural networks (ANN). ANNs were created with up to two hidden layers, varying the number of neurons in each layer. To reduce the number of free parameters in the creation and comparison of the networks, we used only the bipolar sigmoid function as activation function, with a sigmoid *alpha* of 0.5, a *learning rate* fixed in 0.1 and no *momentum*. We also used the early stopping method to track the learning or degeneration of the networks in an attempt to improve generalization.

TABLE I. INPUT/OUTPUT PARAMETERS FOR THE ANNS.

Column	Training Set	Testing Set	p-level
Age	59.99 ± 9.00	59.18 ± 10.22	0.27
Sex	0.68 ± 0.47	0.73 ± 0.45	0.18
BMI	26.99 ± 4.21	27.57 ± 4.01	0.08
Diabetes	0.32 ± 0.47	0.31 ± 0.46	0.60
Glucose	146.37 ± 55.63	145.19 ± 47.94	0.78
Creatinine	1.20 ± 0.48	1.32 ± 0.96	0.06
Reoperation	0.01 ± 0.10	0.03 ± 0.17	0.08
Preserved Ventricular Function	0.79 ± 0.41	0.80 ± 0.40	0.63
Moderated VE Disfunction	0.17 ± 0.37	0.10 ± 0.31	0.02
Important VE Disfunction	0.04 ± 0.21	0.09 ± 0.29	0.01
Mammary bypass	0.96 ± 0.32	0.93 ± 0.32	0.25
Radial bypass	0.01 ± 0.13	0.03 ± 0.23	0.09
Saphenous bypass	1.46 ± 0.85	1.54 ± 0.95	0.31
Total bypasses	2.44 ± 0.85	2.50 ± 0.89	0.36
Extracorporeal circulation	0.69 ± 0.46	0.67 ± 0.47	0.48
Prolonged Mechanical Ventilation (>24h)	0.08 ± 0.26	0.09 ± 0.29	0.52
Reintubation	0.08 ± 0.27	0.08 ± 0.27	0.90
Death (in 30 days)	0.05 ± 0.21	0.11 ± 0.32	0.00

As a second approach, we employed the Bayesian regularization [22] to allow the networks to adjust automatically the number of weights and biases effectively used. We then compared their performance with previous results.

In both cases, all inputs have been scaled to the bipolar sigmoid function interval, in an attempt to avoid synaptic weight overload. Also, training and validation data have been balanced, such that for each outcome, the numbers of positive and negative values were almost equal.

A. Principal Component Analysis

The Principal Component Analysis (PCA) technique [23] can highlight the most relevant information contained in a data set. PCA is a linear transformation that transforms the data to a new coordinate system such that the new set of variables, the principal components, are linear functions of the original variables and are uncorrelated. The technique simplifies data complexity and allows unused or nonrelevant variables to be discarded from the original set. This technique possibly allows the reduction of network complexity (in terms of synaptic connections) and may avoid interference from unused or meaningless data in the network learning and decisioning processes.

TABLE II. PRINCIPAL COMPONENTS.

Component	Eigen-value	Proportion	Accumulated Proportion
1	2.05	0.14	0.14
2	1.98	0.14	0.28
3	1.65	0.11	0.40
4	1.36	0.09	0.50
5	1.19	0.08	0.58
6	1.07	0.07	0.66
7	1.02	0.07	0.73
8	0.90	0.06	0.80
9	0.83	0.05	0.86
10	0.73	0.05	0.91
11	0.66	0.04	0.96
12	0.49	0.03	0.99
13	0.00	0.00	1.00
14	0.00	0.00	1.00

In this study, PCA was performed on the correlation matrix. The correlation matrix is needed when variables in a data set are represented by different units. Once the transformation matrix was computed from the training set, both training and testing sets were projected to the principal component space. This new and transformed data was then fed to new neural networks. We tested different numbers of principal components as input data and also we tested different ANN topologies.

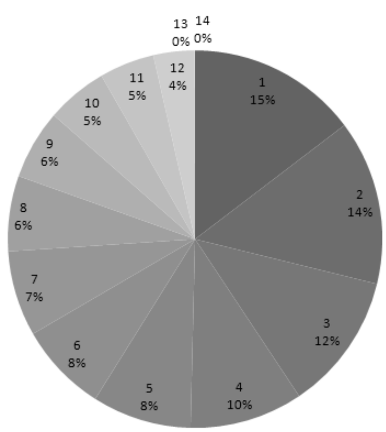

Figure 1. Principal Component Distribution

After applying the analysis, we found that the first four components accounted for approximately 50% of all information contained in our full component data set, and the last 4 accounted for less than 8%, as it is shown in table II and Fig. 1. This could be an indication that network performance could be improved and that ANN complexity could be reduced.

IV. RESULTS AND DISCUSSION

A. Classical approach

We tested 14 neural network configurations for each outcome variable: Prolonged Mechanical Ventilation (PMV); Extracorporeal Circulation (ECC); Reintubation and Death (in 30 days). Table III shows the tested network layer configurations, where *i* is the number of inputs. Without PCA, *i* was always 14, corresponding to the full set of input variables. The best four results of the 56 tests can be seen in table IV. The indicated measured values of sensibility and specificity have been calculated using the highest efficiency cutoff value indicated by their receiver-operating characteristic (ROC) curves.

TABLE III. NETWORK CONFIGURATIONS TESTED.

i-5-1	i-10-10-1
i-10-1	i-10-20-1
i-15-1	i-15-15-1
i-25-1	i-15-25-1
i-50-1	i-20-20-1
i-100-1	i-25-25-1
i-125-1	i-50-50-1

TABLE IV. BEST RESULTS WITHOUT PCA.

Network	Sensibility	Specificity	ROC AUC
ECC	90.85	70.42	82.52
Death	83.33	57.14	71.90
Reintubation	64.71	65.82	68.79
PMV	57.89	78.87	70.73

Training error rates ranged from 0.0491 (ECC) to 0.1163 (Reintubation) and testing rates ranged from 0.0544 (ECC) to 0.1235 (Reintubation). As we can see in table IV, Reintubation and PMV presented the lowest results. This behavior could be caused by inappropriate input data. The principal component distribution indicates that the input dimensionality could be possibly reduced without losing much of the information.

Other tests have been conducted to explore such hypothesis. For these tests we used the projected input data (to the principal component space) as inputs for the neural networks. Different numbers of components have been used in each situation, testing from the first 4 to the first 10 principal components. Again, the same 14 different layer configurations have been tested for each number of components. Table V shows the best 8 results we have found. We can see that the area under the ROC curve (ROC AUC) has increased in at least one test instance for each factor, indicating that both sensibility and specificity had generally improved with the use of PCA.

TABLE V. BEST RESULTS WITH PCA.

Network	Sensibility	Specificity	ROC AUC
ECC-1	83.80	74.65	86.23
ECC-2	80.28	77.46	85.68
Death-1	79.17	68.25	75.21
Death-2	79.17	65.61	74.64
Reintubation-1	70.59	75.00	74.01
Reintubation-2	70.59	77.55	72.84
PMV-1	78.95	60.82	72.73
PMV-2	63.16	70.62	72.59

Comparing only the best ANNs created with and without PCA, the network which benefited the most from the complexity reduction provided by PCA was ECC-1. ECC-1 used only 6 input parameters (the 6 principal components), in a 6-25-1 layer configuration rather than the original 14-15-15-1 configuration used by ECC in table IV. This indicates an expressive reduction of network parameters.

Other networks, however, despite showing improvements in the area under their ROC curve, also had their complexity increased (measured by their number of free parameters - number of connection weights and neuron biases).

The best networks we have found to predict each of the four outcomes were: Death-1, which used only 4 input parameters (the 4 principal components) in a 4-20-20-1 configuration while Death from table IV had a 14-10-20-1 configuration; Reintubation-1, from table V, which used 4 input parameters (the 4 principal components) in a 4-15-25-1 configuration, while Reintubation from table IV which had a 14-10-1 configuration; and finally, PMV-1 from table V, which used 5 input parameters in a 6-20-20-1 configuration, while PMV from table IV had a 14-10-20-1 configuration.

As a side note, despite the improvement of ROC area, training and testing errors remained almost unchanged. Training errors ranged from 0.0549 (ECC) to 0.1197 (Reintubation) and testing errors ranged from 0.0559 (ECC) to 0.1211 (Reintubation).

B. Regularization approach

In a second approach, we employed the Bayesian regularization to allow the networks to automatically adjust their number of weights and biases. This approach should avoid the explorative method used in the first approach. Each network contained only one hidden layer. Table VI shows the initial results considering all inputs in the data set and the effective number of parameters used by each network as reported by the regularization. The suggested number of hidden neurons was calculated considering the total number of used parameters and the number of input and output nodes for each network.

TABLE VI. BEST RESULTS WITH BAYESIAN REGULARIZATION AND WITHOUT PCA.

Network	Effective parameters	Sensibility	Specificity	ROC AUC
ECC	585	84.51	71.83	69.43
Death	587	66.67	67.72	64.94
Reintubation	300	58.82	53.57	57.37
PMV	575	63.16	62.89	65.87

Table VI shows that the ROC AUC decreases when compared with the previous approaches. So do the complexity of ANNs and the effort at determining the best configuration.

After the initial analysis with the full data set, we performed more tests using the PCA technique. Table VII shows only the best results (obtained with PCA technique) and their effective number of parameters as reported by the Bayesian Regularization training algorithm.

TABLE VII. BEST RESULTS WITH BAYESIAN REGULARIZATION AND PCA.

Network	Effective parameters	Sensibility	Specificity	ROC AUC
ECC-1	100	76.06	80.28	71.94
ECC-2	84	82.39	77.46	82.22
Death-1	290	96.77	67.56	73.81
Death-2	391	79.17	66.14	70.55
Reintubation-1	289	64.71	74.49	65.77
Reintubation-2	341	64.71	77.04	67.35
PMV-1	566	89.47	49.48	70.05
PMV-2	566	78.95	60.31	72.21

As it can be seen at Table VII, there is an overall increase in the area in the ROC curve and also a reduction of network parameters when compared with the results of table VI. ECC-2 network used the first 5 components as input data in a suggested 5-12-1 configuration; Death-1 used the first 4 components in a suggested 4-45-1 configuration; Reintubation-2 used the first 5 components in a suggested 5-49-1 configuration; and finally, PMV-2 used the first 5 components in a suggested 5-81-1 configuration.

V. CONCLUSION

With ROC areas generally around 70% and the presence of values higher than 80%, we can say that ANNs can indeed be used in the prognostic evaluation of post-surgery complications in patients that underwent the coronary artery bypass graft surgery. The use of neural networks as decision support systems can improve patient care and surgery planning for patients whose network results indicate need for extracorporeal circulation, prolonged mechanical ventilation, reintubation or even death. In most cases the application of the PCA technique increased their sensibility and specificity rates, but not always contributed for smaller networks, especially when using the classical backpropagation method. The use of regularization techniques, such as the Bayesian regularization, can greatly reduce the effort at finding suitable network configurations when designing a pattern detection system.

ACKNOWLEDGMENT

This research was conducted with financial support by CNPq through the PIBITI institutional (UFSCar) scholarship program.

We are also grateful to the collaboration of Dr. Mauricio Nassal Machado's team from São José do Rio Preto by his precious contribution with the data collection from the Hospital de Base de Sao José do Rio Preto. Without such data, no research could be done.

REFERENCES

[1] J. V. Tu, "Advantages and Disadvantages of Using Artificial Neural Networks Versus Logistic Regression for Predicting Medical Outcomes", J. Clin Epidemiol, v.49, n. 11, p. 1225-1231, 1996

[2] W. G Baxt, "Application of Artificial Neural Networks to Clinical Medicine", *Lancet*, 1995, 346, 1135-1138.

[3] A. Miller, B. Blott, and T. Hames, "Review of Neural Network Applications in Medical Imaging and Signal Processing", *Medical and Biological Engineering and Computing*, 30(5), 449-464, 1992.

[4] A. Miller, *"The Application of Neural Networks to Imaging and Signal Processing in Astronomy and Medicine"*, 1993, Ph.D. thesis, Faculty of Science, Department of Physics, University of Southampton, 1993.

[5] H. Fraser, R. Pugh, R. Kennedy, P. Ross, and R. Harrison, "A Comparison of Backpropagation and Radial Basis Functions, in the Diagnosis of Myocardial Infarction", In: Ifeachor, E., & Rosen, K. (Eds.), *International Conference on Neural Networks and Expert Systems in Medicine and Healthcare*, pp. 76—84, 1994.

[6] D. A. Shoskes, R. Ty, L. Barba and M. Sender, "Prediction of Early Graft Function in Renal Transplantation Using a Computer Neural Network", *Transplant Proc*, v. 30, n. 4, p. 1316-1317, 1998.

[7] P. N. Furness, J. Levesley, Z. Luo, N. Taub, J.I. Kazi, W.D. Bates and M. L. Nicholson, "A Neural Network Approach to the Biopsy Diagnosis of Early Acute Renal Transplant Rejection", *Histopathology*, v. 35, n. 5, p. 461-467, 1999.

[8] S. Simic-Orgrizovic, D. Furuncic, V. Lezaic, D. Radivijevic, R. Blagojevic and L. J. Djukanovic, "Using ANN in Selection of the Most Important Variables in Prediction of Chronic Renal Allograft Rejection Progression", *Transplant Proc*, v. 31, n. 1-2, p. 368, 1999.

[9] D. Sheppard, D. McPhee, C. Darkr, B. Shrethra, R. Moore, A. Jurawitz and A. Gray, "Predicting Citomegalovirus Disease After Renal Transplantation: An Artificial Network Approach", *Int J Med Inf*, v. 54, n. 1, p. 55-76, 1999.

[10] G. Camp-Valls, B. Porta-Oltra, E. Soria-Olivas, J. D. Martin-Guerrero, A. J. Serrano-Lopez, J. J. Perez-Ruixo and N. V. Jimenez-Torres, "Prediction of Cyclosporine Dosage in Patients After Kidney Transplantation Using Neural Networks, *IEEE Trans Biomed Eng*, v. 50, n. 4, p. 442-448, 2003.

[11] R. H. Eckel, "Obesity and heart disease: a statement for healthcare professionals from the Nutrition Committee", *American Heart Association. Circulation*, v.96, p.3248 50, 1997.

[12] P. W. Wilson, R. B. D'Agostino, D. Levy, A. M. Belanger, H. Silbershatz and W. B. Kannel, "Prediction of coronary heart disease using risk factor categories", *Circulation*, v.97, p.1837-47, 1998.

[13] R. C. Lima, L. F. Kubrusly, A. C. S. Nery, B. B. Pinheiro, A. V. Brick, D. S. SOUZA, et al. "Diretrizes da cirúrgia de revascularização miocárdica valvopatias e doenças da aorta", *Arq. Bras. Cardiol.*, v.82 supl.5, 2004.

[14] L. A. Brasil, J. B. Mariano, F. M. Santos, A. L. Silveira, N. Melo, N. G. Oliveira, et al. "Revascularização do miocárdio sem circulação extracorpórea: experiência e resultados iniciais", *Rev Bras Cir Cardiovasc*, v.15, n.1, p.6-15, 2000.

[15] A. C. Fiore, K. S. Naunhein, L. R. McBride, P. S. Peigh, D. G. Pennington, G. C. Kaiser, et al. "Fifteen–year follow-up for double internal thoracic artery grafts", *Eur J Cardiothorac Surg*, v.5, n.5, p.248-52, 1991.

[16] L. A. Brasil, W. J. Gomes, R. Salomao and E. Buffolo, "Inflammatory response after myocardial revascularization with or without cardiopulmonary bypass", *Ann Thorac Surg*, v.66, n.1, p.56-9, 1998.

[17] J. K. Kirklin, S. Westaby, E. H. Blackstone, J. W. Kirklin, D. E. Chenoweth and A. D. Pacifico, "Complement and dramaging effects of cardiopulmonary bypass", *J Thorac Cardiovasc Surg*, v.86, n.6, p.845-57, 1983.

[18] J. Butler, G. M. Rocker and S. Westaby, "Inflamatory response to cardiopulmonary bypass", *Ann Thorac Surg*, v.55, n.2, p.552-9, 1993.

[19] D. Scrutinio and P. Giannuzzi, "Comorbidity in patients undergoing coronary artery bypass graft surgery: impact on outcome and implications for cardiac rehabilitation", *Eur J Cardiovasc Prev Rehabil.*, 15(4):379-85, 2008.

[20] R. V. Freeman, K. A. Eagle, E. R. Bates, S. W. Werns, E. Kline-Rogers, D. Karavite and M. Moscucci, "Comparison of artificial neural networks with logistic regression in prediction of in-hospital death after percutaneous transluminal coronary angioplasty", *American Heart Journal*, 140(3):511-520, 2000.

[21] D. E. Rumelhart and J. L. McClelland, eds., 1986. *Parallel Distributed Processing: Explorations in de Microstructure of Cognition*, vol. 1, Cambridge, MA: MIT Press.

[22] D. J. C. MacKay, Bayesian interpolation. Neural Computation, 4(3), 415-447, 1992.

[23] I. T. Jolliffe, Principal component analysis. New York: Springer Verlag, 1986.