COMPARISON OF ARTIFICIAL NEURAL NETWORK WITH REGRESSION MODELS FOR PREDICTION OF SURVIVAL AFTER SURGERY IN CANCER PATIENTS

2 authors:

Mukunthu Lakshmanan Suresh
Vel Tech - Technical University

Perumal Venkatesan
Sri Ramachandra University

International Journal of Information Science and Computer Mathematics
Volume 1, Number 2, 2010, Pages 137-146
This paper is available online at http://www.pphmj.com

COMPARISON OF ARTIFICIAL NEURAL NETWORK WITH REGRESSION MODELS FOR PREDICTION OF SURVIVAL AFTER SURGERY IN CANCER PATIENTS

M. L. SURESH and P. VENKATESAN

Research Scholar
Sathyabama University
Chennai, India
e-mail: mukunthusuresh@gmail.com

Department of Statistics
Tuberculosis Research Centre
ICMR, Chennai, India
e-mail: venkaticmr@gmail.com

Abstract

Cancer survival prediction in patients who had undergone surgical intervention is an important step in the decision process. The present study investigates the effects of prognostic variables on the breast cancer survival after surgery, over a period of 5-years using feed forward neural network. The neural network was trained and tested using 413 breast cancer patients for the survival prediction with 16 prognostic variables as inputs. The artificial neural network (ANN) proves to be better than regression based models in survival prediction.

1. Introduction

The use of artificial neural networks in biological and medical research has increased enormously in the recent years [11, 17, 20]. ANNs are non linear regressions which have been used in survival prediction and in many bio medical

2010 Mathematics Subject Classification: Kindly Provide.

Keywords and phrases: ANN, FFNN, CART, logistic regression, breast cancer, survival.

Communicated by Kewen Zhao

Received October 29, 2009

research and breast cancer diagnosis [7, 21, 23, 25, 26, 30]. Neural network generalizes from the input data to patterns inherent in the data, and uses these patterns to make predictions. Breast cancer is one of the most common cancers in women [29]. The survival prediction after post surgery breast and lung carcinoma using artificial neural network was analyzed by many authors [10, 13, 19, 22]. For analysis of prognostic factors of patients with cancer, models such as Classification and Regression Trees (CART) and the Logistic Regression (LR) are widely used [9, 12, 16]. The challenge of training the neural network using the clinical data is to extract information hidden in the risk factors at the time of forecast. Recently, neural networks are compared with other statistical methods for survival prediction [2, 6, 14, 15, 24]. This study used artificial neural network for finding the accuracy of survival prediction of breast cancer patients who had undergone surgery and the results are compared with logistic regression and CART.

2. Breast Cancer Data

The data consists of patients registered for suspected breast cancer who had undergone surgery from 2000 to 2003. The descriptions of the database are already given elsewhere [27]. Four hundred and thirteen patients who followed 5 years treatment after breast cancer surgery were considered for this study. The covariates comprise of 16 disease and demographic variables which include age of the patient, age at menarche, age at marriage, number of children, breast feed, age at first child birth, family history, age at menopause, tumor size, nuclear grade, tumor stage, chemotherapy, radiotherapy, hormone therapy, the ratio of the number of positive lymph nodes affected to the total number of nodes examined and post tumor node. Staging index is with 3 grades according to the severity of the tumor, on admission. Some of the prognostic variables are binary. The baseline demographic and disease characteristics of the patients for the three stages are given in Tables 1 and 2.

Table 1. Mean (SD) of covariates according to stage

Variable	Stage II n(143)	Stage III n(251)	Stage IV n(19)	All n(413)
AGE	49.3 (12.5)	48.1 (10.6)	48.8 (11.3)	48.5 (11.3)
AMA	19.7 (5.5)	19.6 (4.9)	19.2 (3.4)	19.6 (5.1)
FCB	21.1 (6.7)	20.5 (7.7)	19.6 (9.5)	20.7 (7.5)
NOC	2.4 (1.1)	2.4 (1.5)	1.6 (1.2)	2.36 (1.4)
TSZ	4.1 (1.6)	7.5 (2.7)	6.8 (1.6)	6.3 (2.8)
RAT	.10 (.17)	.23 (.27)	.26 (.24)	.18 (.25)

Table 2. Distribution of categorical covariates according to stage

Variable		Stage II n(143)	Stage III n(251)	Stage IV n(19)	All n(413)
		%	%	%	%
AMR (<13)		14.0	9.6	5.3	10.9
AMO (>54)		5.0	4.0	0	4.1
NGR	I	24.5	16.3	26.3	19.6
	II	39.2	31.5	47.4	34.9
	III	36.4	52.2	26.3	45.5
FAH (yes)		7.0	7.6	10.5	7.5
BFD (yes)		91.6	85.7	68.4	87.0
CT (yes)		92.3	53.4	89.5	68.5
RT (yes)		92.3	55.0	94.7	69.7
HT (yes)		81.8	32.3	68.4	51.1
PTN (yes)		68.5	76.1	89.5	74.1

The average age and the age at marriage (AMA) were 48.5 and 19.6 years, respectively. The mean tumor size (TSZ) of the breast cancer patients was 6.3cm and the ratio of the positive number lymph nodes was .184. From Table 2, we see that 11% of the patients had the age at menarche (AMR) less than 13 years and 4% of patients have the menopause age (AMO) greater than 54. About 8% of patients have their family members affected by breast caner and 87% of patients had done the breast feeding (BFD). The tumor was present in 74% of patients even after the surgery (PTN).

3. Regression Models

Logistic regression. Regression methods are essential to describe the casual relationship between a response variable and predictor variables. Logistic regression analysis extends the technique of multiple regression analysis to situations in which the outcome variables are categorical. The binary logistic model was used to identify the significant prognostic variables. The goal of the logistic regression analysis is to find the best fitting and the most parsimonious, yet biologically reasonable model to describe the relationship between an outcome variable and a set of independent variables.

The logistic regression model indirectly models the response variable based on probabilities associated with the values of Y. The model is given by

$$\log\left(\frac{p}{1-p}\right) = x_0 + \sum_{i=1}^{n} a_i x_i, \tag{1}$$

where $p = p(Y = 1/X)$. Logistic regression identifies five variables namely, age at marriage, number of children (NOC), tumor size, nuclear grade (NGR) and lymph node ratio (RAT) are the most significant variables for survival beyond 5 years. Hormone therapy (HT) was more effective in treating the breast cancer patients after surgery. The logistic regression resulted in about 71% and 74% correct prediction for survival after 4 and 5 years.

CART. The classification and regression tree methodology is one of the most commonly used techniques in medical applications. Binary trees give an interesting and often illuminating way of looking data in classification and regression problems. A CART is a flexible nonparametric tool for classification and regression problem. The binary tree structured classifiers are constructed by repeated splits of subsets of prognostic variables into descendant subsets beginning with 5th year status [5]. The terminal subsets form a partition of tumor size. Each terminal subset is designed by a class label. There may be two or more terminal subsets with the same class label. The entire construction of tree is revolved around three elements: (i) selection of splits (ii) declare a node as terminal or not and (iii) assignment of terminal node to a class. Figure 1 gives the CART diagram for the breast cancer data. Figure 2 represents the relative importance of covariates.

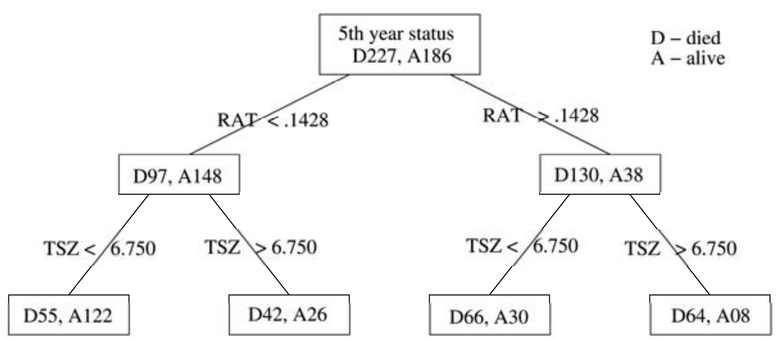

Figure 1. Structure generated by CART at the end of 5th year.

The tree had an initial split on the survival status at the end of the 5th year and 4 terminal subgroups were formed. The variables determining the structure of the tree included were all the breast cancer patient's undergone surgery at the end of the 5th year, the ratio of the number of positive lymph nodes affected to the total number of nodes examined and the tumor size.

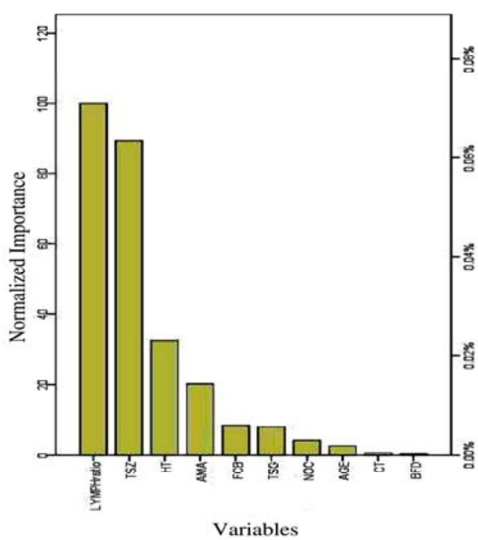

Figure 2. Normalized relative importance of covariates.

The tumor size and the ratio of lymph nodes had 100% and 79.7% as the normalized importance at the 4th year. Number of children and family history (FAH) were the least important factors with 3.1% and .2%, respectively. In the 5th year, the ratio of lymph nodes and tumor size had 100% and 89.3% as the normalized importance. Hormone therapy was significant in treating the patients.

4. Artificial Neural Network

A multilayer perceptron (MLP) is a feed forward neural network (FFNN) with at least one hidden layer. This class of neural networks is used in the most of the applications in medicine and other applications [1, 4, 8, 18]. Multilayer perceptron consists of multiple layers of computational units interconnected in a feed forward manner. In MLP the weighted sum of the inputs and bias term are passed to activation level through a transfer function to produce the output. Multilayer perceptron network uses supervised learning technique and back propagation as error correction method. By using the back propagation algorithm the weights are adjusted until the error becomes negligibly very small. The multilayer perceptron neural network used in this application is shown in Figure 3. The output layer had one output node and one hidden with 9 nodes. The choice of the number of hidden layers, hidden nodes and type of activation function plays an important role in model construction [3, 28].

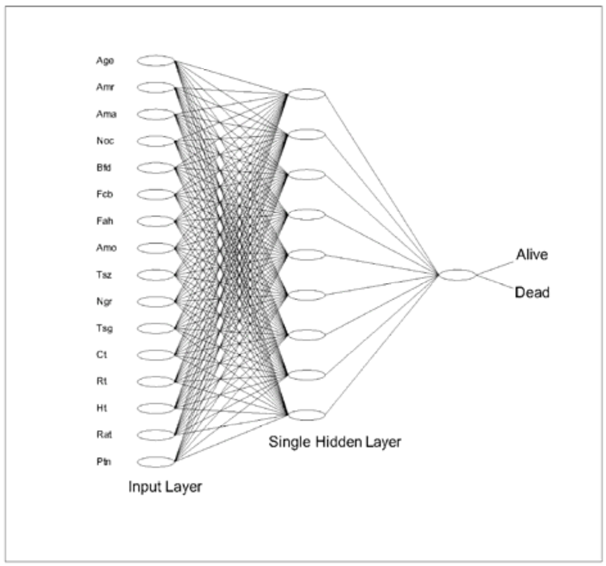

Figure 3. Survival prediction using FFNN.

A multiplayer perceptron using sigmoid function was constructed as shown in Figure 3. To minimize the risk of over fitting and to test the networks generalizing ability, the dataset was divided into training set (70%) and testing set (30%). The training data were used to train the model and the test data were used to test the measure the performance of the network. The output was calculated using

$$y_k = \phi\left(\sum_{h=1}^{H} w_{hk}\,\phi\left(\sum_{i=1}^{l} w_{ik}\,x_i\right)\right), \tag{2}$$

where ϕ is the sigmoid function given by

$$\phi(x) = \frac{1}{1 + e^{-\lambda x}} \tag{3}$$

whose output lies between 0 and 1, and λ is known as the slope parameter. In (2), x_i's are input values, w_{ih} are the weights from input to the hidden layer. The error is calculated using

$$E(w) = \frac{1}{2}[t_k - y_k]^2, \tag{4}$$

where t_k and y_k are target and the output values. The neural network software NeuNet Pro was used to fit the ANN model.

The survival prediction accuracy is given in Tables 3 and 4. The comparative survival prediction for 4th year and 5th year status for the regression models and the neural network is given in Table 5.

Table 3. ANN accuracy measures (4th year)

Actual/Predicted	Dead	Alive	Total	Prediction Error (%)
Dead	66	10	76	13.2
Alive	03	59	62	4.8
Total	69	69	138	9.4
Actual Error (%)	4.4	14.5	9.4	

Table 4. ANN accuracy measures (5th year)

Actual/Predicted	Dead	Alive	Total	Prediction Error (%)
Dead	74	06	80	7.5
Alive	05	52	57	8.8
Total	79	58	137	8.0
Actual Error (%)	6.3	10.3	8.0	

Table 5. Comparative survival prediction of Regression Models and NN

Model/status	LR	CART	NNW
4th year	70.9	67.6	90.6
5th year	73.6	71.2	92.0

5. Discussion

This work attempts to compare the predictive accuracy of the neural network with the regression based approaches. The results show that the ANN model predicts survival after the surgery better than the regression models. The regression model identified age at marriage, number of children, tumor stage, tumor size, nuclear grade and the ratio of lymph nodes as the most significant factors for survival. Hormone therapy was the significant factor in treating the patients. Because of the clinical complexity and pathologic heterogeneity of cancer, correct identification of patients with active disease is unlikely to depend on the presence or absence of a single defining feature. In our study the sensitivity and the specificity for the 4th year survival status are 93% and 81% and for the 5th year are 97% and 78%, respectively. Burke et al. concluded that neural networks are more accurate in predicting the breast cancer than LR and CART models for 5th year survival. Even our findings are similar to [7, 9].

Neural networks have the ability to approximate predictive output to any desirable degree of accuracy when provided with enough running time. This could result in over fitting, particularly when there is an attempt to increase the processing power of the network by adding a large number of hidden neurons. In this case, the network will end up learning not only the training set but also the noise in the data, which leads to poor generalization. Until the model is tested on a different population set, the study can be viewed only as the first attempt in the use of connectionist models in the predictions of breast cancer survival. Our study has several implications regarding the clinical application of artificial neural networks as a diagnostic tool for breast cancer. The use of the neural network could provide physicians and health-care workers with a simple and fast tool with which to assess the survival after surgery for breast cancer. Clinically prognosis is an important indicator to determine the therapies given to the breast cancer patients after surgery. The genetic algorithm can be used along with ANN to improve classification and prediction. Fuzzy neural networks are the other choice when the cancer data are imprecise in nature.

References

[1] H. A. Abbass, An evolutionary artificial neural network approach for breast cancer prognosis, Artificial Intelligence in Medicine 25 (2002), 265-281.

[2] L. Atlas et al., Performance comparisons between back propagation networks and classification trees on three real-world applications, Advances in Neural Information Process Systems 2 (1990), 622-629.

[3] C. M. Bishop, Neural Networks for Pattern Recognition, Oxford University Press, New York, 1995.

[4] L. Bottaci et al., Artificial neural network applied to outcome prediction for colorectal cancer patients in separate institution, Lancet 350 (1997), 469-472.

[5] L. Breiman, J. Friedman, R. Olshen and C. Stone, Classification and Regression Trees, Wadsworth and Brooks, 1984.

[6] H. B. Burke, P. H. Goodman and D. B. Rosen, Comparing the prediction accuracy of artificial neural network and other statistical models for breast cancer survival, Advances in Neural Information Processing Systems 7 (1995), 1063-1067.

[7] H. B. Burke et al., Artificial neural networks improve the accuracy of survival prediction, Cancer 79 (1997), 857-862.

[8] J. A. Cruz, D. S. Wishart, Application of machine learning in cancer prediction and prognosis, Cancer Informatics 2 (2006), 59-77.

[9] D. Delen, G. Walker and A. Dadam, Predicting Breast cancer survivability: a comparison of three data mining methods, Journal of Artificial Intelligence in Medicine 34 (2005), 113-127.

[10] J. A. Gomez-Ruiz, J. M. Jerez-Aragones, J. Munoz-Perez and E. Alba-Conejo, A neural network based model for prognosis of early breast cancer, Applied Intelligence 20(3) (2004), 231-238.

[11] Sarah. L. Gulliford, Steve Webb, Carl G. Rowbottom, David W. Corne and David P. Dearnaley, Use of artificial neural network to predict biological outcomes for patients receiving radical radiotherapy of the prostate, Radiotherapy and Oncology 71(1) (2004), 3-12.

[12] Kenneth R. Hess, Marie C. Abbruzzese, Renato Lenzi, Martin N. Raber and James L. Abbruzzese, Classification and regression tree analysis of 100 consecutive patients with unknown primary carcinoma, Clin. Cancer Res. 5 (1999), 3403-3410.

[13] M. F. Jefferson et al., Comparison of a genetic algorithm neural network with logistic regression for predicting outcome after surgery for patients with nonsmall cell lung carcinoma, Cancer 79 (1997), 1338-1342.

[14] J. M. Jerez-Aragones et al., A combined neural network and decision trees model for prognosis of breast cancer relapse, Artificial Intelligence in Medicine 27 (2003), 45-63.

[15] Imran Kurt, Mevlut Ture and A. Turhn Kurum, Comparing performances of logistic regression, classification and regression tree and neural networks for predicting coronary artery disease, Expert Systems with Applications 34 (2008), 366-374.

[16] E. T. Lee, Statistical Methods for Survival Data Analysis, John Wiley and Sons, New York, 2003.

[17] Paulo J. Lisoba, Azzam F. G. Taktak, The use of artificial neural network in decision support in cancer: a systematic review, Neural Networks 19(4) (2006), 408-415.

[18] P. J. Lisoba, T. A. Etchells, I. H. Jarman, M. S. Hane Aung, S. Chabaud, T. Bachelot, D. Perol, T. Gargi, V. Bourdes, S. Bonnevay and S. Negrier, Time-to-event analysis with artificial neural networks: an integrated analytical and rule-based study for breast cancer, Neural Networks 21(2-3) (2008), 414-426.

[19] P. J. Lisoba et al., A Bayesian neural network approach for modeling censored data with an application to prognosis after surgery for breast cancer, Artificial Intelligence in Medicine 28 (2003), 1-25.

[20] J. E. Montie and J. T. Wei, Artificial neural networks for prostate carcinoma risk assessment: an overview, Cancer 88(12) (2000), 2655-2660.

[21] R. N. Naguib et al., Artificial neural network in cancer research, Pathobiology 65(3) (1997), 129-139.

[22] P. M. Ravdin and G. M. Clark, A practical application of neural network analysis for predicting outcome of individual breast cancer patients, Breast Cancer Research and Treatment 22 (1992), 285-293.

[23] R. M. Ripley, A. L. Harris and O. L. Tarassenko, Non linear survival analysis using neural network, Statistics in Medicine 23 (2004), 825-842.

[24] P. B. Snow et al., Neural network and regression prediction of 5-year survival after colon carcinoma treatment, Cancer 91(8 suppl) (2001), 1673-1678.

[25] P. Venkatesan and S. Anitha, Application of a radial basis function neural network for diagnosis of diabetes mellitus, Current Science 91 (2006), 1195-1199.

[26] P. Venkatesan and M. L. Suresh, Neural network model for classifying renal failure, P. Balasubramaniam and R. Uthayakumar, eds., Computing and Mathematical Modeling, Appl. Publishers, (2007), 150-160.

[27] P. Venkatesan and M. L. Suresh, Breast cancer survival prediction using artificial neural network, International Journal of Computer Science and Network Security 9(5) (2009), 169-174.

[28] H. White, Artificial Neural Networks: Approximation and Learning Theory, Blackwell, Cambridge, MA, 1992.

[29] P. A. Wingo, T. Tong and S. Bolden, Cancer statistics, CA Cancer J. Clin. 41 (1995), 8-30.

[30] Y. Wu et al., Artificial neural networks in mammography: application to decision-making process in the diagnosis of breast cancer, Radiology 187 (1993), 81-87.