

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Prediction and prognosis of acute myocardial infarction in patients with previous coronary artery bypass grafting using neural network model

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SUMMARY

Introduction/Objective The aim of this study was to analyze the usefulness and accuracy of artificial neural networks in the prognosis of infarcted patients with previous myocardial surgical revascularization.

Methods The 13 predictor variables per patient were defined as a data set. All the patients were divided into two groups randomly: the training group and the test group, of 1090 patients each. The evaluation of the neural network performance was organized by using the original data, as well as the complementary test data, containing patient data not used for training the network. In generating the file of comparative results, the program compared the actual outcome for each patient with the predicted one.

Results All the results were compared with 2×2 contingency table constructed from sensitivity, specificity, accuracy, and positive-negative prediction. The network was able to predict the outcome with the accuracy of 96.2%, sensitivity of 78.4%, specificity of 100%, positive predictivity of 100%, and negative predictivity of 96%. There was not efficient prognosis of infarcted patients previously operated on using linear discriminant analysis (accuracy 68.3%, sensitivity 66.4%, and positive predictivity 30.2%).

Conclusion This study suggest that a neural network was better for almost all parameters in outcome prognosis of infarcted patients with previous myocardial surgical revascularization.

Keywords: artificial intelligence; prognosis; acute myocardial infarction; revascularization

INTRODUCTION

Patients with previous coronary artery bypass grafting (CABG) represent a substantial percentage of the total population of patients with acute myocardial infarction (AMI) [1, 2, 3]. The timing of CABG for AMI remains a controversial topic [4–7]. The benefit persist in most patients during the first few years after surgery, but the progression of coronary artery disease in the ungrafted coronary arteries and the development of atherosclerosis in the vein grafts are important mechanisms by which angina and/or myocardial infarction can recur, detracting from the primary effect of revascularization [3, 7, 8, 9].

Prognosis of the future disease expression is an important part in the follow-up of patients with previous CABG. Prognosis can be expressed in symptom-free period, quality of life, but the most common type of prognosis is survival. Linear discriminate analysis, multilinear regression analysis, and logistic regression analysis have been used extensively for evaluation in medical prognosis. It is well known that outcome of patients with previous CABG is influenced by many abnormalities. In processing medical classification, linear methods cannot be appropriate because many medical patterns can

be classified only by more complex nonlinear decision making. Each of these methods has inherent limitations when applied to a complex biological process, and a high degree of predictive accuracy has yet to be achieved.

Neural networks are a form of artificial intelligence and may obviate some of the problems associated with traditional statistical techniques, and they represent a major advance in predictive modeling [10–13]. Neural networks can find seemingly hidden features in input patterns, not visible by conventional statistical methods. There are some studies that have shown that connectionist models can be used for the prediction of outcome in patients with coronary heart disease, the onset of diabetes, and other medical problems [14–19].

The aim of this study is to analyze the usefulness and accuracy of an artificial neural network in AMI expression and its five-year prognosis in patients with previous CABG, using a complex mixture of predictor variables.

METHODS

The baseline characteristics and clinical data were recorded in 2180 consecutive patients (13.8% women, mean age 63.4 ± 4 years) with previous

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CABG who were later determined to have a definite AMI. The patients with early perioperative AMI were excluded from the study. The diagnostic parameters and protocol were identical for all the patients. For inclusion, the patients were required to have at least two of the three following criteria: chest discomfort and/or symptoms suggestive of myocardial infarction lasting ≥ 20 minutes, electrocardiography changes suggestive of evolving myocardial infarction according to the Minnesota coding system, and typical elevation of at least one of three cardiac enzymes to at least twice the upper limit of the normal reference range. The follow-up period was 13.8 years (range 1.5–15). Information regarding survival (new coronary event – NCE) or circumstances of death during the follow-up period was obtained by control clinical examination or by letter or telephone interview.

Predictor variables

The data set contained 13 predictor variables per patient (Table 1). All the patients were divided into two groups randomly, the training group and the test group, each containing 1090 patients. The original data included five continuous predictor variables [age, body mass index (BMI), C/T index, number of grafts, and ejection fraction] and eight binary predictors (sex, history of hypertension, smoking, hypercholesterolemia, diabetes mellitus, previous angina pectoris, previous AMI, and type of previous AMI) (Table 1). For use by the neural network, all the input variables were automatically standardized into the interval [0, 1] (Table 1).

Table 1. Clinical variables and input nodes

Clinical variables (n = 13)	No. of input nodes (n = 14)
1. Sex (male) (yes/no)	1
2. Age (< 40 years, 40–65 years, 65 years)	2
3. Hypertension (yes/no)	1
4. Smoking (yes/no)	1
5. Hypercholesterolemia (yes/no)	1
6. High BMI (yes/no)	1
7. Diabetes mellitus (yes/no)	1
8. Previous angina (yes/no)	1
9. Previous AMI (yes/no)	1
10. Q-wave previous AMI (yes/no)	1
11. No. of grafts > 1 (yes/no)	1
12. Enlarged C/T index (yes/no)	1
13. EF $\leq 40\%$ (yes/no)	1

BMI – body mass index; AMI – acute myocardial infarction; EF – ejection fraction

Neural network architecture

The artificial neural network was created using commercial desktop PC software Neural Planner 4.5, running under Microsoft Windows (Microsoft Corporation, Redmond, WA, USA). Inputs into the neural network included 13 clinical variables, giving a total of 14 input nodes (variable age was standardized as binary variable) (Table 1). The neural network had 29 hidden nodes in one layer. The layer of 29 hidden nodes is a layer that connects only to the output

nodes. There were six output nodes: AMI expression after CABG (yes/no), time interval from CABG to AMI (≤ 5 years after CABG, > 5 years after CABG), localization of AMI (anterior, inferior, lateral) after CABG, type of AMI (Q wave, non-Q wave AMI), and time of cardiac death expression after AMI (in the first, second, third, fourth, or fifth year of the follow-up period), if NCE was expressed in the follow-up period. All six outcomes after a five-year observation period were coded as follows: 0 = free of NCE; 1 = non-free of NCE. Patients were randomly enrolled into the test group or the training group. The learning method was error backpropagation and the transfer function was sigmoid. The method of presentation of examples during the training was randomized and the method of weight updating was continuous.

Artificial neural network performance was evaluated using the original data set for each network, as well as its complementary test data set, containing patient data not used for training the network. Generating a file of comparative results, program compared each patient's actual outcome with the predict one. At the end, the results from this file were analyzed and compared, on the basis of a 2×2 contingency table constructed from expected or obtained statistics (accuracy, sensitivity, specificity, and positive/negative predictivity), as well as on the basis of receiver operating characteristic (ROC) areas [20, 21].

Ethical approval for this study was obtained from the Cardiology Clinic Review Board, Clinical Center of Serbia (approval number 1973/2020)

RESULTS

The study group included 2180 consecutive patients (301 female, 1879 male), age range being 26–82 years, mean age 63.4 ± 4 years, divided into training and testing sets. Clinical characteristics of patients in training and testing sets are shown in Table 2.

Table 2. Clinical characteristics of patients in training and testing sets

Clinical variable	Training set (n = 1090)	Testing set (n = 1090)	P
Sex (male)	952 (87.3%)	861 (79%)	0.0001
Age < 40 years	2 (0.2%)	8 (0.7%)	0.0572
Age 40–65 years	856 (78.5%)	821 (75.4%)	0.0966
Age 65 years	232 (21.3%)	261 (23.9%)	0.1098
Hypertension	370 (33.9%)	382 (35%)	0.5887
Smoking	162 (14.9%)	240 (22%)	0.0001
Hypercholesterolemia	510 (46.8%)	571 (52.4%)	0.0090
High BMI	229 (21%)	207 (19%)	0.2388
Diabetes mellitus	290 (26.6%)	305 (28%)	0.4708
Previous angina	468 (42.9%)	414 (38%)	0.0185
Previous AMI	500 (45.9%)	371 (34%)	0.0001
Previous Q wave AMI	457 (41.9%)	391 (36%)	0.0037
No. of grafts > 1	796 (73%)	730 (67%)	0.0020
Enlarged C/T index	205 (18.8%)	245 (22.5%)	0.0343
EF $\leq 40\%$	135 (12.4%)	168 (15.4%)	0.0411

BMI – body mass index; AMI – acute myocardial infarction; EF – ejection fraction

Table 3. Prognosis of new coronary event expression: linear discriminant analysis

Output variables	Data set	Accuracy (%)	Sensitivity (%)	Specificity (%)	Positive predictivity (%)	Negative predictivity (%)
1. AMI expression after CABG	Full set	68.3	66.4	68.8	30.2	90.4
2. Time-interval from CABG to AMI	Full set	66.8	63.8	65.2	26.8	88.2
3. Localization of AMI	Full set	62.8	60.2	60.4	22.4	84
4. Type of AMI	Full set	65.6	64	65.2	24.6	86.6
5. Time of cardiac death expression after AMI	Full set	60.8	60.4	62.2	20	80.2

AMI – acute myocardial infarction; CABG – coronary artery bypass grafting

Table 4. Prognosis of new coronary event expression: neural network analysis

Output variables	Data set	Accuracy (%)	Sensitivity (%)	Specificity (%)	Positive predictivity (%)	Negative predictivity (%)
1. AMI expression after CABG	Training set	96.2	78.4	100	100	96
	Test set	86.2	56.2	96.3	68	92
2. Time-interval from CABG to AMI	Training set	100	100	100	100	100
	Test set	88.6	72	90.2	60.5	94
3. Localization of AMI	Training set	93.8	73.4	98.7	90.2	96
	Test set	84	34.2	90.6	48.6	88
4. Type of AMI	Training set	96.8	86.0	100	100	96
	Test set	76.6	44.8	84.2	36.3	86
5. Time of cardiac death expression after AMI	Training set	98	100	100	100	100
	Test set	82.8	46.4	84.2	34.2	48.2

AMI – acute myocardial infarction; CABG – coronary artery bypass grafting

Statistical analysis

The results of univariate statistical analysis of study variables are shown in Table 2. Categorical variables significantly different between training and testing sets were sex, smoking, hypercholesterolemia, previous angina, previous AMI, previous Q wave AMI, number of grafts more than one, enlarged C/T index, and ejection fraction $\leq 40\%$.

The linear discriminate analysis (Table 3) was not efficient enough to distinguish NCE expression; the accuracy for AMI expression after CABG was only 68.3%, with the sensitivity of 66.4%; for the time-interval from CABG to AMI, the accuracy was 66.8%, with sensitivity of 63.8%; for the localization of AMI, the accuracy was 62.8%, with sensitivity of 60.2%; for the type of AMI, the accuracy was 65.5%, with sensitivity of 64%; and for the time of cardiac death expression after AMI, the accuracy was only 60.8%, with sensitivity of 60.4%. The weakest feature of the linear discriminate analysis solution was positive predictivity, which was only 30.2% for AMI expression after CABG; 26.8% for the time-interval from CABG to AMI; 22.4% for the localization of AMI; 24.6% for the type of AMI; and only 20% for the time of cardiac death expression after AMI. Negative predictivity was excellent for AMI expression after CABG (90.4%), for the time-interval from CABG to AMI (88.2%), for the localization of AMI (84%), for the type of AMI (86.6%), and for the time of cardiac death expression after AMI (80.2%). These results show that a statistical linear model is not able to perform class separation in multidimensional space and that a nonlinear approach is justified.

Neural network analysis

The artificial neural network results are summarized in Table 4. The network was able to predict outcome with the accuracy of 96.2% for AMI expression after CABG for the training data set vs. 86.2% for the test data set, with a sensitivity of 78.4% vs. 56.2%, specificity 100% vs. 96.3%, positive predictivity 100% vs. 68%, and negative predictivity 96% vs. 92%. For the time-interval from CABG to AMI, the network was able to predict the outcome with the accuracy of 100% for the training data set vs. 88.6% for the test data set, with a sensitivity of 100% vs. 72%, specificity 100% vs. 90.2%, positive predictivity 100% vs. 60.5%, and negative predictivity 100% vs. 94%. For the localization of AMI, the network was able to predict the outcome with the accuracy of 93.8% for the training data set vs. 84% for the test data set, with a sensitivity of 73.4% vs. 34.2%, specificity 98.7% vs. 90.6%, positive predictivity 90.2% vs. 48.6%, and negative predictivity 96% vs. 88%. For the type of AMI, the network was able to predict the outcome with the accuracy of 96.8% for the training data set vs. 76.6% for the test data set, with a sensitivity of 86% vs. 44.8%, specificity 100% vs. 84.2%, positive predictivity 100% vs. 36.3%, and negative predictivity 96% vs. 86%. For the time of cardiac death expression after AMI, the network was able to predict the outcome with the accuracy of 98% for the training data set vs. 82.8% for the test data set, with a sensitivity of 100% vs. 46.4%, specificity 100% vs. 84.2%, positive predictivity 100% vs. 34.2%, and negative predictivity 100% vs. 48.2%. The least reliable variable for all outcome variables was always sensitivity, denoting a relative inability to correctly predict the number of patients with different NCE expressions.

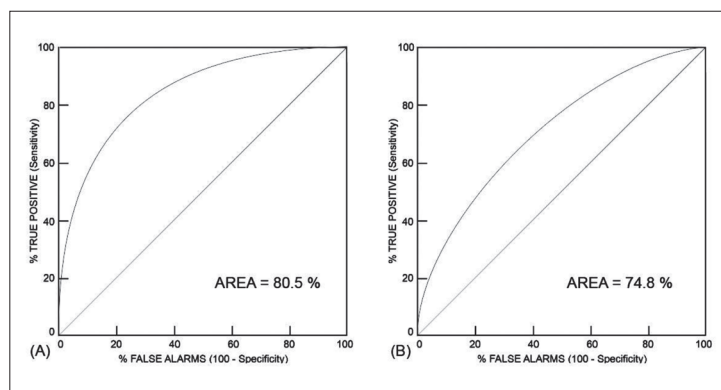


Figure 1. Receiver operating characteristic curve for committee classifier; (A) area (C-index) for neural network analysis 80.5%; (B) area (C-index) for linear discriminant analysis 74.8%

The ROC areas (C-index) for both prediction models after training (using training data) and final testing (using testing data) are provided in Figure 1. ROC areas (C-index) are all about 74.8% for logistic regression and vary 1.4 percentage points (range 73.4–76.2%). For artificial neural network model, ROC areas (C-index) are all about 80.5% and vary 1.5 percentage points (range 79–82%).

DISCUSSION

The performance of artificial neural networks in the prognosis of acute myocardial infarction in patients with previous CABG can be rated as very good if we consider that a large number of input variables is associated with outcome and input variables present a large variability among patients of the training and the testing set. The number of training examples may be too low in relation to problem dimensionally, but large enough for very good accuracy and specificity of artificial neural network analysis. In particular, the accuracy will increase with the increase in the number of training sets and the number of hidden layers. A nearly optimal combination of high sensitivity and specificity was achieved with the network model for time interval from CABG to AMI variable [22, 23, 24]. The accuracy value of 88.6% achieved with the test data demonstrates that this neural network was able to give a decision surface with acceptable prognostic power for the prediction of the time interval for AMI expression after CABG. In analyzing the performance of the neural network and linear discriminate analysis in outcome prognosis of AMI in patients with previous CABG, it is clear that neural network was better for almost all parameters in outcome prognosis for all analyzed variables.

Some of the previous studies have shown that ACS patients with prior CABG have an increased risk of early mortality. In the Global Registry of Acute Coronary Events (GRACE), prior CABG was associated with increased in-hospital mortality [26] and was a univariable predictor of

six-month mortality [25, 26]. The same results were presented with the neural network prediction model in our study.

Prior CABG was an independent predictor of cardiovascular death, AMI, and heart failure. The GRACE registry findings proved the findings of an earlier Canadian cohort study of 410 AMI patients with or without prior CABG. In these patients, a history of CABG was associated with a higher crude rate of ischemic cardiac events at five years [27, 28]. Our prognostic model has shown very similar results in the five-year interval prediction. Some other previous studies have demonstrated that patients with prior CABG have more extensive native vessel coronary artery disease [28]. The higher expression of previous

AMI and left ventricle dysfunction in patients with prior CABG may explain the reduced capacity of these patients to withstand recurrent myocardial ischemia or infarction and their increased risk of cardiac morbidity and mortality [28].

As in our study, the VALIANT (Valsartan in Acute Myocardial Infarction) trial also showed that a history of prior CABG was a univariable but not a multivariable predictor of all-cause mortality [29]. This result is consistent with similar results from the GRACE registry [25].

It's well known that a major problem among artificial neural network is overtraining [30, 31]. Because of that, when an artificial neural network is overtrained, it models the test group so well that it becomes poor at predicting outcomes when new cases are presented. This problem in prediction and prognosis of AMI in patients with previous CABG was probably resolved with a relatively high number of analyzed patients and long follow-up period. Further prospective validation of this neural network approach, with a more prolonged follow-up period, may be useful.

CONCLUSION

In this clinical situation, artificial intelligence appears to be superior to linear methods for prediction and prognosis of AMI in patients with previous CABG.

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Примена неуронских мрежа у предвиђању појаве акутног инфаркта миокарда код болесника са претходном хируршком реваскуларизацијом миокарда

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САЖЕТАК

Увод/ Циљ Циљ ове студије је да испита сензитивност и специфичност неуронских мрежа у предвиђању појаве акутног инфаркта миокарда код болесника са претходном хируршком реваскуларизацијом миокарда.

Метод Скуп података се састоји од 13 предиктивних параметара по болеснику. Посматрани болесници подељени су у две групе: група болесника за обучавање неуронске мреже (1090 болесника) и група болесника за тестирање неуронске мреже (1090 болесника). Неуронска мрежа је обучавана употребом оригиналних података за сваки појединачни параметар, док је њена специфичност и сензитивност тестирана новим сетом оригиналних података болесника који нису коришћени за обучавање неуронске мреже.

Резултати На крају испитивања, резултати обучавања неуронске мреже контролисани су мерењем прецизности, сензитивности, специфичности и позитивне/негативне предиктивности. Неуронска мрежа приказала је статистички

значајне вредности у прогнози ових болесника са тачношћу од 96,2%, сензитивношћу од 78,4%, специфичношћу 100%, позитивним предвиђањем 100% и негативним предвиђањем 96%. Линеарна дискриминантна анализа, као статистички модел предвиђања и прогнозе појаве акутног инфаркта миокарда код оперисаних болесника, показала се као лошији предиктивни модел у поређењу са неуронском мрежом (тачност 68,3%, сензитивност 66,4%, позитивно предвиђање 30,2%).

Закључак Анализирањем употребе неуронске мреже у предвиђању појаве и прогнозе акутног инфаркта миокарда код болесника са претходном хируршком реваскуларизацијом миокарда показало се јасно да је неуронска мрежа бољи предиктивни модел у односу на све статистичке параметре који се користе за анализирање предиктивних параметара.

Кључне речи: вештачка интелигенција; прогноза, акутни инфаркт миокарда; реваскуларизација