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

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

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SUMMARY

Introduction/Objective The aim of this study was to analyze the usefulness and accuracy of artificial neural network in the prognosis of infarcted patients with operation.

Methods The thirteen predictor variables per patient were defined as data set. All patients were divided in two groups randomly: training group of 1090 patients and test group of 1090 patients. Evaluation of neural network performance was organized by using of the original data, as well as its complementary test data, containing patient data not used for training the network. Generating a file of comparative results, program compared actual with predict outcome for each patient.

Results All results were compared with 2x2 contingency table constructed from sensitivity, specificity, accuracy and positive-negative prediction. Network was able to predict outcome with accuracy of 96.2%, sensitivity of 78.4%, specificity 100%, positive predictivity 100% and negative predictivity 96%. There was not efficient for prognosis of infarcted patients with operation using linear discriminant analysis (accuracy 68.3%, sensitivity 66.4%, and positive predictivity 30.2%).

Conclusion This study suggest that neural network was better for almost all parameters in outcome prognosis of infarcted patients with operation.

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

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.

Методе Дата сет се сатоји 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%, позитивном предвиђању 100% и негативном предвиђању 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 боесника 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

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 controversial subject [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 influenced with a lot of abnormalities. In process of medical classification, linear methods can`t be appropriate because many medical patterns can be classified only by more complexes, 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 they may obviate some of the problems associated with traditional statistical techniques, and they are representing a major advance in predictive modeling [10–13]. Neural networks can find hidden features in input patterns that are not visible by conventional statistical methods. There are some studies that have shown that using of connectionist models for prediction of outcome in patients with coronary heart disease [14, 15], the onset of diabetes [16, 17] and other medical problems [18, 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±4.0 years) with previous CABG who were late 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 patients. For inclusion, patients were required to have at least two of the three following criteria: chest discomfort and/or symptoms suggestive of myocardial infarction for ≥ 20 minutes, ECG 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 normal. The follow-up period was 13.8 years (range 1.5 to 15). Information regarding survival (new coronary event) or circumstances of death during follow-up period was obtained by control clinical examination or by letter or telephone interview.

Predictor variables

The data set contains 13 predictor variables per patient (Table 1). All patients were divided in two groups randomly: training group of 1090 patients and test group of 1090 patients. The original data included 5 continuous predictor variables (age, body mass index (BMI), C/T index, number of grafts and ejection fraction) and 8 binary predictors (gender, 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 input variables were automatically standardized into the interval [0, 1] (Table 1).

Neural network architecture

The artificial neural network was created using the commercial software program "Neural Planner 4.5" runs on a desktop personal computer under Microsoft Windows. 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 1 layer. The layer of 29 hidden nodes is a layer that connects only to the output nodes. There were 6 output nodes consisting of 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 1st, 2nd, 3rd, 4th or 5th year of follow-up period), if it's expressed as new coronary event (NCE) in follow-up period. All 6 outcomes after a 5-year observation period were coded as follows: 0 = free of NCE; 1 = non-free of NCE. Patients were randomly divided to the testing or training group. Learning method was back propagation of errors and transfer function was sigmoid. Method of presentation of examples during training was randomized and method of weight updating 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 actual with predict outcome for each patient. At the end, results from this file were analyzed and compared, on the basis of a 2x2 contingency table constructed from expected or obtained statistics (accuracy, sensitivity, specificity and positive/negative predictivity), as well as on the basis receiver operating characteristics (ROC) areas [20, 21].

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

RESULTS

The study group included 2180 consecutive patients (301 female, 1879 male), range 26 to 82 years old, mean 63.4±4.0 years, divided in training and testing sets. Clinical characteristics of patients in training and testing sets are shown in Table 2.

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 gender, smoking, hypercholesterolemia, previous angina, previous AMI, Q-wave previous AMI, number of grafts more than 1, enlarged C/T index and ejection fraction equal or smaller than 40%.

The linear discriminate analysis (Table 3) was not efficient enough to distinguish NCE expression, and accuracy for AMI expression after CABG was only 68.3%, with a sensitivity of 66.4%; for time-interval from CABG to AMI was 66.8%, with sensitivity of 63.8%; for localization of AMI accuracy was 62.8%, with sensitivity of 60.2%; for type of AMI 65.5%, with sensitivity of 64% and for time of cardiac death expression after AMI 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 time-interval from CABG to AMI; 22.4% for localization of AMI; 24.6% for type of AMI and only 20% for time of cardiac death expression after AMI. Negative predictivity was excellent for AMI expression after CABG (90.4%), for time-interval from CABG to AMI (88.2%), for localization of AMI (84%), for type of AMI (86.6%) and for 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. Network was able to predict outcome with accuracy for AMI expression after CABG of 96.2% 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 time-interval from CABG to AMI, network was able to predict outcome with 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 localization of AMI, network was able to predict outcome with 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 type of AMI, network was able to predict outcome with 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 time of cardiac death expression after AMI, network was able to predict outcome with 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 worst variable for all outcome variables was always sensitivity, denoting a relative inability to predict correctly the number of patients with different NCE expressions.

The receiver operating characteristic (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% to 76.2%). For artificial neural network model, ROC areas (C-index) are all about 80.5% and vary 1.5 percentage points (range, 79.0% to 82.0%).

DISCUSSION

The performance of artificial neural networks in the prognosis of acute myocardial infarction in patients with previous coronary artery bypass grafting can be rated as very good if we considered that a large number of input variables were associated with outcome and input variables presented large variability among patients of the training and testing set. The number of training examples was may be too low in relation to problem dimensionally, but was enough for a very good accuracy and specificity of artificial neural networks analysis. In particular, the accuracy will increase with the increase in the number of training set 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 prediction of time-interval for AMI expression after coronary artery bypass grafting. In analyzing the performance of 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 previous studies have shown that ACS patients with prior CABG have an increased risk of early mortality. In the GRACE registry [25], prior CABG was associated with increased in-hospital mortality [26] and was a univariable predictor of 6-month mortality [25]. The same results were presented with 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 those of an earlier Canadian cohort study in 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 5 years [27, 28]. Our prognostic model had shown very similar results in 5 years prediction time-interval. Some other previous studies have demonstrated that patients with prior CABG have more extensive native vessel CAD [28]. The higher expression of previous AMI and LV 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 trial [29] also shown that a history of prior CABG was a univariable but not a multivariable predictor of all-cause mortality. 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 over trained, 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 probably was resolved with relatively enough number of analyzed patients and long follow-up period. Further prospective validation of this neural network approach, with 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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Conflict of interest: None declared.

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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

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

Clinical variable	Training set (n=1090)	Testing set (n=1090)	p Value
Sex (male)	952 (87.3%)	861 (79%)	0.0001
Age <40 years	2 (0.2%)	8 (0.7%)	0.0572
40–65 years	856 (78.5%)	821 (75.4%)	0.0966
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
Q-wave previous 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 ≤ 40%	135 (12.4%)	168 (15.4%)	0.0411

Table 3. Prognosis of NCE 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

Table 4. Prognosis of NCE 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	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

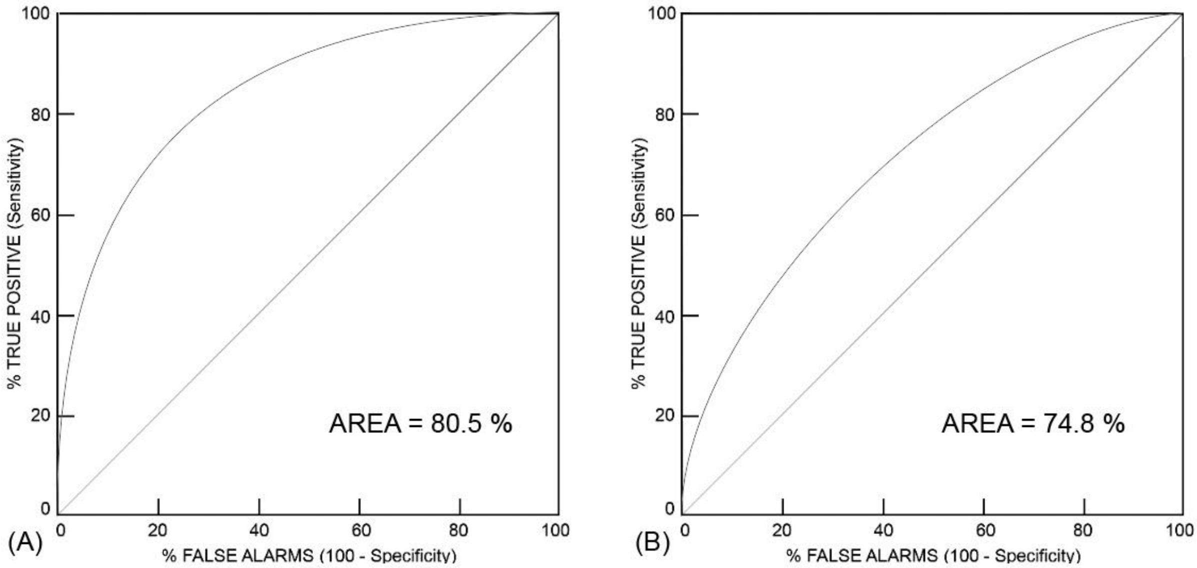

Figure 1. Receiver operating characteristic curve for committee classifier. (A) Area (C-index) for Neural network analysis 80.5%; (B) Area (C-index) for linear discriminant analysis 74.8%