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Method of Predicting the Probability of Restenosis after Coronary Artery Stenting.

Stanislav Ivanovich Sivakov*, Valeriy Mihailovich Nikitin, and Yuriy Ivanovich Afanasiev.

Belgorod State National Research University, 85 Pobedy St., Belgorod, 308000, Russia.

ABSTRACT

The article outlines the results of investigation of the effect of biochemical analyses and stenosis location on probability of restenosis after coronary stenting operation on the basis of which a method for predicting the probability of restenosis after coronary artery stenting was elaborated by means of reverse stepwise regression with the aid of Statistica 7.0 software.

Keywords: restenosis, coronary arteries, reverse stepwise regression, prediction.

Corresponding author

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INTRODUCTION

Russia nowadays holds the leading place in regard to number of cardiovascular diseases as compared to the countries in Europe and America. Total mortality from such diseases in our country makes 57%. Currently the Russian government gives increased consideration to this problem and allocates corresponding financial resources which evidences significance and relevancy of investigations in this sphere [1].

Use of the latest scientific achievements both in the sphere of medicine and of systematic analysis and mathematical modeling is one of the principal factors for prevention of various human diseases inclusive of cardiovascular and their consequent effective treatment. Formulation of adequate prognostic mathematic models of diseases onset and behavior will give an opportunity to proceed to formal description of the diagnosis development process and of the method ensuring the best results for healing [2].

Restenosis is one of the cardiovascular system diseases, it is a repeated heart vessel constriction after coronary stenting operation. At present there are a number of investigations focused at elaboration of new methods for diagnostics of restenosis [3,4]. But the major part of the investigations deals with design of materials and coatings for stents in order to reduce the probability of repeated constriction of the vessel lumen (restenosis) inside the stent [5,6]. Nevertheless there is always the risk of repeated vessel lumen constriction (restenosis) inside the stent.

Today there are a number of studies related to development of mathematical models for predicting heart vessel restenosis [7-9]. The following disadvantages can be distinguished relatively to them:

- They do not allow quantifying restenosis probability (Patent RU #2395091, published: 20.07.2010, Patent RU #2349919 published: 20.03.2009).
- Application restriction by gender (Patent RU #2410019, published: 27.01.2011).
- Insufficiently high confidence of a prognosis due to absence of interrelationship between constriction rate and the value of prognostic coefficient of restenosis probability inside the stent (Patent RU #2410019, published: 27.01.2011).

The investigation task consists in creation of a method of predicting the probability of restenosis for an extended range of possible clinical situations after coronary artery stenting for various categories of patients in order to reduce the error of prediction of the disease onset.

The previous investigations carried out by the composite author allowed to determine a correlation of restenosis rate with the biochemical blood assay results (prothrombin ratio, atherogenicity index, very little density lipoproteins), restenosis rate and location as well as to establish differencies in the model behavior for various stenosis locations. [10]

METHODOLOGY

With a view to the investigation there was developed a methodology for realization of the experiment which could be divided into the following stages:

1. Forming of a representative experimental sample W^e [W_1^e ,W_2^e …W_{58}^e], where W_q^e – examination results (biochemical assay results BC_{iq}^e , location and rate of stenosis S_q^e and restenosis R_q^e) of the q-th patient (q=1…58), who experiences the coronary stenting operation was performed according to the following stages:

2. As of the moment of stenting t_q the patient's blood is being sampled and for each W_q^e the biochemical assay result values in physical terms are being recorded: BC_{1q}^e – prothrombin ratio PTR, BC_{2q}^e –

atherogenicity index, BC_{3q}^{e} – very little density lipoproteins (VLDLP), BC_{4q}^{e} – high density lipoproteins (HDLP). Where: t_q – moment of stenting of the *q*-th patient.

3. The values of the biochemical assay results are being normalized in accordance with the following formula:

$$BC_{iq} = \frac{2BC_{iq}^{e} - BC_{imax}^{e} - BC_{imin}^{e}}{BC_{imax}^{e} - BC_{imin}^{e}},$$

where BC_{iq}^{e} – value of the *i*-th biochemical assay for W_q^e (*i = 1…4),* BC_{imax}^{e} – maximum value of the *i*-th biochemical analysis within sample W^e , BC_{imin}^{e} – minimum value of the *i*-th biochemical analysis within sample W^e .

4. Determination of the affected vessel diameter of (d_{sq}^{e}), vessel lumen diameter (d_{0q}^{e}) and the vessel lumen diameter after stenting (D_{0q}^{e}) as of the moment of time t_q for each W_q^e .

5. For each W_q^e stenosis rate S_q^e is calculated according to the following formula:

$$S_q^e = (d_{sq}^{e} / d_{0q}^{e}),$$

6. The stenosis rate value for each W_q^e was normalized with use of the following formula:

$$S_q = \frac{2S_q^e - S_{\max}^e - S_{\min}^e}{S_{\max}^e - S_{\min}^e},$$

where S_q^e – stenosis rate value W^e , $S_{\max}^e$ – maximum stenosis rate value within sample W^e , $S_{\min}^e$ – minimum stenosis rate value within sample W^e ,

7. 6 months after the operation the stented vessel lumen diameter (D_{sq}^{e}).was determined for each W_q^e .

8. Stenosis rate R_q^e was calculated for each W_q^e according to the following formula:

$$R_q^e = (D_{sq}^{e} / D_{0q}^{e}),$$

MAIN BODY

The extent of a representative experimental sample W^e includes 58 cases of coronary vessel stenting. 6 months after the operation a repeated examination was performed in order to monitor repeated constriction of the heart vessels (restenosis). Disease locations in question: the obtuse marginal branches, the circumflex artery, the right coronary artery, the front interventricular artery. The investigation was carried out in the premises of the Belgorod Regional Clinical Hospital.

In that way a model for calculation of the prognostic coefficient of probability of restenosis development 6 months after operation was designed. The model is represented by four equations for each location respectively. Every equation has a second-order logic and is represented as follows:

$R = K_0 + K_1*S + K_2*BC_1 + K_3*BC_2 + K_4*BC_3 + K_5*BC_4 + K_6*S^2 + K_7*BC_1^2 + K_8*BC_2^2 + K_9*BC_4^2 + K_{10}*BC_2*S + K_{11}*BC_3*S + K_{12}*BC_4*S + K_{13}*BC_1*BC_2 + K_{14}*BC_1*BC_3 + K_{15}*BC_3*BC_4$,

where BC_1 – prothrombin ratio PTR, BC_2 – atherogenicity index, BC_3 – very little density lipoproteins (VLDLP), BC_4 – high density lipoproteins (HDLP), K_i – coefficient which value depends on stenosis location (i=1,2,…,15),

All of the coefficients were determined by means of reverse stepwise regression with use of Statistica 7.0 software package for statistical analysis:

1. In case of stenosis location in the obtuse marginal branches the coefficients assume the following values: $K_0 = -1007.3013$; $K_1 = 7.8604$; $K_2 = 18{,}4524$; $K_3 = -18.4524$; $K_4 = 0$; $K_5 = 491.274$; $K_6 = 0$; $K_7 = 0$; $K_8 = 0$; $K_9 = 0$; $K_{10} = 0$; $K_{11} = 0$; $K_{12} = -6.5503$; $K_{13} = 0$; $K_{14} = 0$; $K_{15} = 0$.

2. In case of stenosis location in the circumflex artery the coefficients assume the following values: $K_0 = -3670.7068$; $K_1 = -168.876$; $K_2 = 177.2463$; $K_3 = 944.4897$; $K_4 = -40.4895$; $K_5 = 0$; $K_6 = 1.1258$; $K_7 = -0.7408$; $K_8 = 0$; $K_9 = 0$; $K_{10} = 0$; $K_{11} = 0$; $K_{12} = 0$; $K_{13} = -10.0989$; $K_{14} = 0$; $K_{15} = 0$.

3. In case of stenosis location in the right coronary artery the coefficients take the following values: $K_0 = -129.2103$; $K_1 = 2.1992$; $K_2 = -4.1480$; $K_3 = 303.8618$; $K_4 = -522.1097$; $K_5 = -619.0743$; $K_6 = 0$; $K_7 = 0.0269$; $K_8 = -10.6126$; $K_9 = 0$; $K_{10} = 19.3059$; $K_{11} = 6.3003$; $K_{12} = 0$; $K_{13} = 0$; $K_{14} = 0$; $K_{15} = 42.9024$.

4. In case of stenosis location in the front interventricular artery the coefficients take the following values: $K_0 = 6434.5551$; $K_1 = -170.2915$; $K_2 = 2.6731$; $K_3 = -466.8056$; $K_4 = 1484.8251$; $K_5 = 0$; $K_6 = 0$; $K_7 = 0$; $K_8 = 0$; $K_9 = 0$; $K_{10} = 6{,}2234$; $K_{11} = -14.9416$; $K_{12} = 0$; $K_{13} = 0$; $K_{14} = -3.8507$; $K_{15} = 0$.

CONCLUSION

Equivalence of the predicted restenosis rate 6 months after stenting operation with the confidence level $p=0.05$ according to Fisher's ratio test is guaranteed for the following intervals:

- For stenosis located in the circumflex artery $R \in [0;40]$;
- For stenosis located in the obtuse marginal branches $R \in [0;50] \cup [90;100]$;
- For stenosis located in the right coronary artery $R \in [0;50]$;
- For stenosis located in the front interventricular artery $R \in [0;100]$.

FINDINGS

On the basis of this investigation the method of predicting of the heart vessels restenosis after coronary stenting operation was designed. Besides, the Federal Intellectual Property Agency made a decision on issuance of a patent for invention with application of the mentioned method.

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