Ways to optimize the prediction of vascular events in patients with acute coronary syndrome and atherosclerotic lesions of the renal arteries

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Abstract. Using the logistic regression equations obtained during the work, forecast tables were developed to assess the risk of developing vascular events in the long term. The proposed forecasting model is an independent method for assessing the risk of fatal and non-fatal vascular events. The consistency of the model has a scientific and practical justification. The proposed original risk model can be used in a comprehensive examination of patients with acute coronary syndrome and atherosclerotic lesions of the renal arteries.

1. Introduction

Predicting the course of diseases in patients is one of the important and difficult tasks that practicing cardiologists solve. An assessment of the risk of life-threatening cardiovascular events makes it possible to identify patients with a low and high risk of complications and death[1].

At low risk, routine outpatient drug therapy is usually performed to control symptoms and slow organ damage. In cases of a high risk of complications and death, active drug therapy is indicated, often in the intensive care unit, as well as invasive treatment [2,3].

The assessment of the prognosis of diseases and the corresponding treatment tactics are included in almost all modern recommendations for the treatment of cardiovascular diseases. [4]. Convenient tools for assessing risks in clinical practice are special scales that quantify the risk of adverse events. There is a tendency to use scales as mandatory diagnostic tools, along with traditional laboratory tests. [5, 6]. Scales are developed on the basis of analysis of data from large groups of patients with an assessment of the frequency of development of cardiovascular events and death during long-term follow-up. The scales usually include well-studied, easily identifiable indicators of the patient’s health status. Using mathematical methods, for example, regression analysis, the most significant factors for forecasting are selected and a scale adapted for practice is constructed [7].

In order to evaluate the effectiveness of a predictive system, C-statistics is usually used, which includes an estimate of the area under the ROC (receiver operating characteristic) curve. The ROC curve is a function of the frequency of true positive results (sensitivity) versus the frequency of false positive results (100 specificity). Each point of the ROC curve represents a sensitivity / specificity pair corresponding to the accepted threshold [8,9]. The area under the curve (AUC) allows you to evaluate how well the scale distinguishes between diagnostic groups. C-statistics <0.7 characterizes an inadequate distinction between data, a value from 0.7 to 0.8 is acceptable, and from 0.8 to 0.9 an excellent distinction [10,11].
2. Methods
The study included 323 patients with acute coronary syndrome who were treated in the cardiology department of the regional vascular center, of which 217 (67.1%) were men, 106 (32.9%) were women. The average age of the examined patients was 59.6 ± 9.2 years.

All patients underwent standard biochemical studies, including the assessment of lipid metabolism: total cholesterol; high and low density lipoprotein cholesterol; atherogenic index; triglycerides, creatinine and urea levels.

The complex of instrumental studies included recording ECG at rest, Holter ECG monitoring, ultrasound of the heart, ultrasound examination of the kidney, coronary angiography to assess the degree of damage to the coronary vessels, selective angiography of the renal vessels.

Statistical analysis of the results was carried out using a set of applied statistical programs Microsoft Office Excel 2010 (Microsoft Corp., USA) and STATISTICA 10.0 (StatSoft Inc., USA). In order to assess the type of data distribution, Kolmogorov-Smirnov analysis was used; for values of p > 0.05, the distribution was considered not different from the normal one.

Descriptive statistics were carried out to determine the following features: the data were presented as M ± SD (M is the arithmetic mean, SD is the standard deviation) with a normal distribution and in the form Me [Q1; Q3] (Me is the median, Q1 and Q3 are the first and third quartiles) with abnormal distribution. In the normal distribution of the sample, when comparing two independent samples, the Student criterion was used, and when different from the normal one, the Mann-Whitney test and χ2 or the Leuven test with the determination of F. We also used logistic regression analysis with the calculation of relative risks (OR) and determination χ2, the relationship was considered statistically significant at a value of p < 0.05.

ROC analysis with the construction of operational characteristic curves and the calculation of the curve area coefficient (AUC) was used to assess the predictive information content of the methods used.

3. Results
In a two-factor logistic regression analysis, stenosis of the renal arteries or bilateral stenosis of the renal arteries was chosen as one factor, as the other signs that previously demonstrated their influence on the risk of developing vascular events. Atherosclerotic lesions of the renal vessels together with the size of the ejection fraction or size, left atrium, right ventricle, and also the thickness of the interventricular septum influenced the risk of non-fatal vascular events (χ2 = 7.46, p = 0.024; χ2 = 7.37, p = 0.025; χ2 = 11.1, p = 0.004; χ2 = 9.52 p = 0.009, respectively). Also, the discussed risk increased in the case of an increase in Δ GFR after coronary angiography, χ2 = 9.83, p = 0.007 (table 1).

| Another clinical symptom | Assessment stenosis/ another sign | Odds ratio, stenosis / another sign | Odds ratio, stenosis / other trait | χ2 | Degree of freedom | P  |
|--------------------------|----------------------------------|------------------------------------|-----------------------------------|----|------------------|----|
| Throw Faction            | 0.99 / -0.05                     | 2.69 / 0.95                        | 2.69 / 0.10                       | 7.46 | 2                | 0.024 |
| Left pres                | 0.92 / 0.11                      | 2.51 / 1.12                        | 2.51 / 12.44                      | 7.37 | 2                | 0.025 |
| Right ventricle          | 1.36 / 0.17                      | 3.91 / 1.19                        | 3.91 / 2609                       | 11.1 | 2                | 0.004 |
| Interventricular         | 0.89 / 0.17                      | 2.43 / 2.43                        | 2.43 / 9.52                       | 9.52 | 2                | 0.009 |
The obtained logistic regression equations made it possible to develop forecast tables, one of which is presented as an example in table 2.

**Table 2**- Forecast table for assessing the risk of non-fatal vascular events depending on the presence of renal artery stenosis and the value of the left atrium

| Left atrium, mm and renal artery stenosis | 38 | 40 | 42 | 44 | 46 | 48 | 50 | 52 | 54 |
|-----------------------------------------|----|----|----|----|----|----|----|----|----|
| The amount of risk, %                   |   |    |    |    |    |    |    |    |    |
| Left atrium, mm and no renal artery stenosis | 38 | 40 | 42 | 44 | 46 | 48 | 50 | 52 | 54 |
| The amount of risk, %                   |   |    |    |    |    |    |    |    |    |

According to the findings of echocardiography, it was found that in the presence of renal vascular stenosis and left atrium size = 38 mm, the risk of non-fatal vascular events was 11%, with left atrium size = 46 mm, this risk was 24%, while in patients without renal vascular lesions - 3% and 9%, respectively. When the ejection fraction = 60% in the examined patients with renal vascular stenosis, the risk discussed was 17%, while the ejection fraction = 45% was 37%, while in patients without atherosclerotic lesion of the renal vessels, these indicators were - 6% and 21%, respectively.

When factors such as renal artery stenosis and the size of the right ventricle are included in the risk table, the probability of developing non-fatal vascular events can reach 84%, while in patients without renal vascular damage this indicator was significantly lower and amounted to 63%. When analyzing cardiovascular risk in patients with atherosclerotic lesions of the renal arteries and interventricular septum thickness = 12 mm, the specified risk is 9%, in patients without lesion - 5%, with interventricular septum thickness = 20 mm - 28% and 15%.

In the course of the work, it was found that among patients with renal vascular stenosis and Δ GFR of 60 ml / min / 1.73 m2, the risk of developing non-fatal vascular events was 57%, while in patients without renal artery disease, it was 14% (table 3).

**Table 3**- Prediction table for assessing the risk of developing non-fatal vascular events depending on the presence of renal artery stenosis and Δ GFR.

| Δ GFR and renal artery stenosis | -80 | -60 | -40 | -20 | 0  | 20 | 40 | 60 | 80 |
|---------------------------------|-----|-----|-----|-----|----|----|----|----|----|
| The amount of risk, %           | 3   | 5   | 7   | 9   | 15 | 27 | 38 | 57 | 75 |
The presence of bilateral renal vascular stenosis, as well as a number of signs, such as the size of the left atrium, thickness of the interventricular septum, and total blood cholesterol increased the risk of fatal vascular events (table 4).

**Table 4** - Logistic regression analysis of the effect of bilateral renal artery stenosis and other clinical signs on the risk of fatal vascular events

| Another clinical symptom | Assessment stenosis/another sign | Odds ratio, stenosis / another sign | Odds ratio, stenosis / other symptom | \( \chi^2 \) | Degree of freedom | P  |
|--------------------------|--------------------------------|-----------------------------------|-------------------------------------|---------|-----------------|---|
| Left atrium              | 1,22 / 0,09                   | 3,44 / 1,1                        | 3,44 / 8,7                          | 6,43    | 2               | 0,04 |
| Interventricular septum  | 1,24 / 0,13                   | 3,25 / 1,14                      | 3,25 / 256                          | 7,96    | 2               | 0,018 |
| Total cholesterol        | 1,35 / 0,12                   | 0,86 / 1,13                      | 0,86 / 6,17                         | 6,59    | 2               | 0,037 |

So, the risk of developing fatal vascular events in patients with bilateral renal artery stenosis and a total cholesterol value of 6 mmol / L was 42%, in patients without renal vascular stenosis - 11% (table 5). If the total cholesterol value is increased to 10 mmol / L, the discussed risk is 54 and 16%, respectively.

**Table 5** - Forecast table for assessing the risk of fatal vascular events depending on the presence of bilateral renal artery stenosis and the value of total cholesterol

| Total cholesterol, mmol / L and bilateral renal artery stenosis | 6       | 8       | 10      | 12      | 14      | 16      |
|--------------------------------------------------------------|---------|---------|---------|---------|---------|---------|
| The amount of risk,% | 42      | 47      | 54      | 59      | 65      | 72      |

| Total cholesterol, mmol / L and no renal artery stenosis | 6       | 8       | 10      | 12      | 14      | 16      |
|----------------------------------------------------------|---------|---------|---------|---------|---------|---------|
| The amount of risk,% | 11      | 13      | 16      | 19      | 22      | 27      |
with bilateral renal artery disease and interventricular septum thickness = 12 mm was 28%, while in patients without renal vascular stenosis this risk was 6%.

During a two-factor logistic analysis, it was found that bilateral damage to the renal arteries, as well as factors such as stages of chronic kidney disease (p = 0.034, $\chi^2 = 6.78$), glomerular filtration rate before angiography (p = 0.0001, $\chi^2 = 18.3$), as well as the severity of stenosis of the proximal and distal sections of the anterior interventricular branch (p = 0.005, $\chi^2 = 10.6$) (p = 0.027, $\chi^2 = 7.2$) influenced the risk of fatal and non-fatal vascular events.

Analysis of the obtained evidence showed that patients with bilateral renal vascular disease and stage 2 chronic kidney disease had a 32% fatal and non-fatal vascular event risk; in patients without renal vascular stenosis, the risk discussed was 12%.

It was also found that in patients with bilateral renal artery damage and the presence of hemodynamically significant stenosis in the proximal section of the anterior interventricular branch, this risk was 63%, while in patients without renal artery damage, the risk was 8%. In patients with hemodynamically significant damage to the middle third of the anterior interventricular branch and bilateral renal artery stenosis, the risk of developing fatal and non-fatal vascular events was 49%, in patients without renal vascular stenosis - 7%.

In the course of the work, a ROC analysis was carried out, during which the informativeness of the forecasting tools for the endpoints discussed above was separately analyzed: non-fatal vascular events, fatal vascular events and fatal / non-fatal vascular events. In relation to the first endpoint, a combination of signs: the presence of renal artery stenosis, ejection fraction, sizes of the left atrium, right ventricle, thickness of the interventricular septum, Δ GFR allowed to increase AUC to 0.78, increasing the sensitivity of the technique to 75%, while maintaining specificity at the level of 70% (Figure 1).

![Figure 1](image1.png)

**Figure 1.** ROC-curve sensitivity / specificity for renal artery stenosis, parameters of echocardiography and Δ GFR (CKD-EPI) in predicting the risk of non-fatal vascular events

ROC analysis of the influence of factors on fatal vascular events showed a higher informativity than during the analysis discussed above. The combination of such factors as the presence of bilateral renal vascular stenosis, the size of the left atrium, the thickness of the interventricular septum and the value of total blood cholesterol made it possible to increase the AUC to 0.93, the sensitivity of the method to 82%, and the specificity to 95%. (Figure 2).
Figure 2. ROC-curve sensitivity / specificity for bilateral renal artery stenosis, sizes of LP and MJP and level of cholesterol in predicting the risk of developing non-fatal vascular events.

The combined point of the presence of bilateral renal vascular stenosis, the stage of chronic kidney disease, the severity of proximal and middle UCW stenosis showed an AUC of 0.92, with a sensitivity of 90% and a specificity of 90% (Figure 3).

Figure 3. ROC curve sensitivity / specificity for bilateral renal artery stenosis, stages of CKD and the severity of stenosis of the proximal and middle sections of the UML in predicting the risk of fatal and non-fatal vascular events.

4. Discussion
With the introduction of interventional diagnostic methods into practical cardiology, the definition of tactics for treating a patient with acute coronary syndrome and prediction of cardiovascular risk has become the most successful and effective 8-11. Among people with renal artery stenosis, there is a very high risk of fatal and non-fatal cardiovascular events 12.

According to the literature we have analyzed to date, no methods have been proposed to predict outcomes in the long term in the group of patients under discussion.

The proposed forecasting method is based on the fact that, using an adequate mathematical apparatus, a complex of factors was determined that affect the risk of developing fatal and non-fatal vascular events in patients with acute coronary syndrome and atherosclerotic lesion of the renal arteries.

Using the logistic regression equations obtained during the work, forecast tables were developed to assess the risk of developing vascular events in the long-term period.

5. Conclusion
The proposed forecasting model is an independent method for assessing the risk of fatal and non-fatal vascular events. The consistency of the model has a scientific and practical justification. The proposed
original risk model can be used in a comprehensive examination of patients with acute coronary syndrome and atherosclerotic lesions of the renal arteries.

Acknowledgements
The study had no sponsorship.

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