**Kravchun PG, Ryndina NG, Tytova G.Yu., Borovik K.M., Yermak O.S.**

**Gensini score as a marker of the coronary artery atherosclerotic lesions severity and its relation with galectin-3 concentration in patients with acute myocardial infarction and abdominal obesity**

**Introduction.** Despite the improvement and progressive development of diagnostic and therapeutic approaches, ischemic heart disease (IHD) is one of the leading causes of morbidity and mortality worldwide. According to data published by WHO in 2012, more than 7.4 million fatal cases of coronary heart disease were registered, accounting 31% of the total mortality from noncommunicable diseases [1].

A number of traditional scales, such as the GRACE (Global Registry of Acute Coronary Events), the TIMI (Thrombolysis in Myocardial Infarction) scale, are currently used as objective non-invasive means for assessing the severity of coronary artery disease [2-4]. At the same time, engaging in routine practice of new parameters is considered as a promising direction of modern medicine. So some cardial markers, such as the creatine phosphokinase MB fraction, troponin I and T, are common in the daily work of health facilities as indicators of early diagnosis and stratification of risk in IHD patients.

Galectin-3, which is a member of the family of β-galactoside-binding lectins, is expressed by various types of cells, including almost all immunocompetent cells, namely, macrophages, monocytes, eosinophils, mast cells, natural killers, activated T- and B-lymphocytes [5]. Galectin-3 is localized in the cytoplasm of cells and structures located near the nucleus, in addition, it is secreted on the cell surface and in the biological fluid. The extracellular galectin-3 modulates the cell-cell, cell-extracellular matrix relationship. Thus, this parameter is involved in cell differentiation, fibrosis and immune-inflammation [6].

Information on changes in the activity of the galectin-3 concentration in patients with acute forms of IHD, namely acute myocardial infarction (AMI), is contradictory. In patients with AMI, expression of galectin-3 levels is associated with an increasing activity of immune-inflammatory factors [7-9]. At the same time, Singsaas et al. demonstrated that the expression of galectin-3 levels did not significantly change in acute period of AMI and no relationship was found between the concentration of this indicator and ischemic myocardial damage [10]. The results obtained by Szadkowska et al. indicate that galectinemia is associated with a recurrence of myocardial infarction in the early post-infarction period [11]. On the other hand, there is information on the inclusion of the family of galeсtines in the progression of adipocytic tissue growthening [12-15]. Insufficiently studied for today is the question of the possibility of attracting the activity of galectin-3 to the atherosclerotic process, taking into account its participation in the processes of immune inflammation.

The aim is to study the state of the coronary arteries in patients with acute myocardial infarction and concomitant obesity by angiography and an assessment of the presence and character of the relationship between atherosclerotic lesions of coronary arteries, calculated by Gensini score, and the concentration of galectin-3.

Materials and methods of research

The study involved 31 patients with AMI and concomitant obesity at the age of 58.42 ± 3.27 years who were treated in the infarction department of the Kharkiv City Clinical Hospital №27. This cohort of patients was performed angiography of the coronary arteries with the subsequent stenting of the infarction-dependent coronary artery within 12 hours from the onset of pain syndrome.

The diagnosis of AMI was established on the basis of clinical and anamnestic and laboratory-instrumental studies using the criteria recommended by the European Society of Cardiologists in 2017 for STEMI. The presence of obesity was established according to the WHO classification, 1997 under the body mass index (BMI)> 30 kg/m2, which was determined by the formula: BMI (kg/m2) = body weight/high2. All patients had obesity of the abdominal type. Galectin-3 was determined using the Human Galectin-3 ELISA Kit (China). The degree of severity of coronary atherosclerosis by angiography of the coronary arteries was determined using the Gensini scale. Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis as follows: 1 point for ≤25% narrowing, 2 points for 26 to 50% narrowing, 4 points for 51 to 75% narrowing, 8 points for 76 to 90% narrowing, 16 points for 91 to 99% narrowing, and 32 points for total occlusion. Thereafter, each lesion score is multiplied by a factor that takes into account the importance of the lesion's position in the coronary circulation (5 for the left main coronary artery (Left main)), 2.5 for the proximal segment of the left anterior descending coronary artery (LAD), 2.5 for the proximal segment of the circumflex artery, 1.5 for the mid-segment of the LAD, 1.0 for the right coronary artery (RCA), the distal segment of the LAD, the posterolateral artery, and the obtuse marginal artery, and 0.5 for other segments). Finally, the Gensini score was calculated by summation of the individual coronary segment scores. Hemodynamically significant stenoses are evaluated with a percentage of stenosis ≥70 %, ≥50 % for the left main coronary artery.

Criteria for exclusion were acute and chronic inflammatory processes, Q-negative acute myocardial infarction, diffuse connective tissue disease, neoplastic processes, concomitant diseases of the thyroid gland, and the presence of symptomatic hypertension.

The received data is presented as the arithmetic mean value and the statistical error of the arithmetic mean (M±m). An assessment of the differences between groups in a distribution close to normal was carried out using the Student's criteria. The presence of links is established using the Spirman correlation. Statistical significance was considered to be discrepancy at p <0,05.

Results and discussion.

In patients with AMI and obesity, according to the angiography of the coronary arteries, a single- vessel lesion was found in 13 people (40.7%), multi-vessel coronary lesion - 18 (59.3%). The number of affected vessels ranged from 1 to 4. In 19 (61.3%) patients with AMI with concomitant obesity, according to angiographic examination, a combined arterial artery scarring was found. The most frequent combination of lesions in the RCA, LAD and circumflex artery was observed in 8 cases (25.8%). The analysis of the frequency of major coronary artery lesions has shown that the most commonly occurring was atherosclerotic lesion of LAD (89% of cases). The second place is RCA - 59,3%, about half of patients with AMI and obesity (48,1%) had a defeat of circumflex artery. The left main coronary artery was the least frequently affected in patients with AMI with concomitant obesity - 11%.

In the study of the results of angiography, it was found that all major arteries found both hemodynamically significant and hemodynamically insignificant stenoses. The data is presented in Table 1.

Table 1. Frequency of coronary artery disease in patients with AMI and obesity

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Left main coronary artery | LAD | Circumflex | RCA |
| Hemodynamically significant stenosis,% | 33 % | 69,3 % | 42,1 % | 60,9 % |
| Hemodynamically insignificant stenosis,% | 67 % | 30,7 % | 57,9 % | 39,1 % |

In LAD and RCA, hemodynamically significant stenoses were more often detected, while in the circumflex and the left main coronary artery the proportion of hemodynamically insignificant stenoses was of great advantage.

The greatest exposure of LAD was accompanied by the presence of the highest mean values of stenoses - 77.3%. The results are presented in Table 2.

Table 2. Average values of stenoses in the group of patients with AMI and obesity

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Patients with AMI and obesity (n=31) | | | |
| Left main coronary artery | LAD | Circumflex | RCA |
| Average value of stenosis in groups,% | 60 % | 77,3 % | 62,5 % | 68,2 % |
| Mean value of hemodynamically significant stenoses,% | 89 % | 89 % | 84,4 % | 87,4 % |
| Mean value of hemodynamically insignificant stenoses,% | 45 % | 47,5 % | 48,2 % | 42,2 % |

As can be seen from Table 1 and 2, in the second place, both by frequency and by degree of defeat, is RCA, with an average stenosis of 68.2%. In some ways, there was lower degree of stenosis of the circumflex and the left main coronary artery, where the average stenosis values were 62.5% and 60% respectively. The average value of hemodynamically significant stenoses was not significantly different in patients with AMI and obesity, depending on the localization of the lesion and fluctuated within 84.4 - 89%. Similar results were obtained in the study of the mean value of hemodynamically insignificant stenoses, which did not differ significantly in patients with varying localization of the lesion.

Table 3 presents data on infarction-dependent coronary arteries in patients undergoing AMI and concomitant obesity. The development of the majority of AMI, namely 57.1%, was due to the occlusion of LAD.

Table 3. Infarction-dependent coronary arteries in patients with AMI and obesity

|  |  |  |
| --- | --- | --- |
|  | Patients with AMI and obesity (n=31) | |
| Number of cases | % |
| LAD | 18 | 57,1 % |
| RCA | 9 | 28,6 % |
| Left main coronary artery | 1 | 3,6 % |
| Circumflex | 3 | 10,7 % |

Among the major arteries, RCA and circumflex with fewer cases of Left main coronary artery were less often infarction-dependent.

In the analysis of the localization of the defeat of the infarction-dependent coronary arteries, it was found that the most frequent occlusion is located in the proximal and middle parts of the arteries (60.7 and 25% respectively), the less involved in the pathological process were distal parts - 14.3% of cases. The data is presented in Table 4.

Table 4. Localization of defeat in infarction-dependent coronary artery in patients with AMI and obesity

|  |  |  |
| --- | --- | --- |
| Localization in the coronary arteries | Patients with AMI and obesity (n=31) | |
| Number of cases | % |
| Proximal part | 19 | 60,7 |
| The middle part | 8 | 25 |
| Distal part | 4 | 14,3 |

In order to evaluate the changes in parameters reflecting coronary artery defects according to angiography in patients with AMI and obesity, we have divided the data of the above mentioned parameters according to quartile of galectin-3 concentrations. The results are presented in Table 5.

Table 5. Status of coronary arteries in patients with AMI and obesity, depending on the concentration of galectin-3 (M ± m)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Indicator,  unit of measurement | Concentration of galectin-3 in patients with AMI and obesity | | | |
| 1 quartile  8,81 – 16,48 ng/ml | 2 quartile  16,49 – 23,47 ng/ml | 3 quartile  23,48 – 29,87 ng/ml | 4 quartile  29,87 – 41,42 ng/ml |
| 1 | 2 | 3 | 4 |
| Number of affected vessels | 1,25±0,16 | 1,83±0,40  р1та 2>0,05 | 2,43±0,37  р1та 3<0,01  р2та 3>0,05 | 2,86±0,40  р1та 4<0,01  р3та 4>0,05 |
| The number of affected segments | 1,50±0,19 | 3,17±1,01  р1та 2 = 0,07 | 3,29±0,71  р2та 3>0,05  р1та 3 <0,05 | 4,01±0,82  р1та 4<0,01  р3та 4>0,05 |
| Scale Gensini, points | 22,13±0,88 | 33±2,91  р1та 2 = 0,06 | 56±5,27  р2та 3<0,05  р1та 3 <0,01 | 76,57±6,34  р1та 4<0,01  р3та 4<0,05 |

In patients with AMI and obesity when comparing 1 quartile with 3 and 2 quartiles, no significant difference was found in the number of affected vessels. Similar results were obtained by comparing 2 and 3 quartile of galectin-3 levels, as well as 3 and 4 quartiles of the galectin-3 concentration. Comparison of vascular lesions in patients with AMI and obesity of 1 quartile and quartile 3 showed a significant difference in the increasing of this parameter in 3 quartile of galectin-3 concentration (p<0.01). As regards the comparison of 1 and 4 quartiles of the galectin-3 levels, there are likely differences in the growth of the affected vessels number in 4 quartile of the galectin-3 levels (p<0.01).

There was a tendency to increase the number of affected segments in patients with AMI and obesity in 2 quartile of galectin-3 levels compared to 1 quartile, which did not reach probability (p = 0.07).

The number of affected segments in 3 and 4 quartiles reliably exceeded this in 1 quartile of galectin-3 levels (p<0.05 and p<0.01 respectively). When comparing the number of affected segments either between 2 and 3 quartiles, or 3 and 4 quartiles, no probable changes were detected (p>0.05).

Gensini scale points, reflecting the severity of atherosclerotic damage in coronary vessels, were higher in patients with AMI and obesity in 2 quartile of galectin-3 concentration versus quartile 1, but received changes reflect a trend that did not reach the level of probability (p=0.06). A comparison of the number of the Gensini scale points in patients with 2, 3, and 4 quartiles has established their significant increase in proportion to the increase in quartile of galectin-3 levels (p<0,05). It was determined that in patients with AMI and obesity in both 3 and 4 quartiles, Gensini scale scores were significantly higher than those in 1 quartile of galectin-3 levels (p<0.01).

Correlation has been used to assess the presence and character of the links between the concentration of galectin-3 and the parameters reflecting coronary artery lesions (number of injured vessels/segments, Gensini score) in patients with AMI and obesity.

In patients with AMI and obesity, a strong direct correlation was found between the concentration of galectin-3 and the Gensini scale (r=0.72; p<0.05), the number of affected vessels (r=0.69; p<0.05), the number of affected segments (r=0.71; p<0.05).

In patients with AMI and obesity included in 1 and 2 quartile of galectin-3 concentrations, direct correlations of milde strength between galectin-3 and the number of affected vessels were found (r=0.45; p<0.05 for 1 quartile and r=0.51; p<0.05 for 2 quartile), the number of affected segments (r=0.49; p<0.05 and r=0.53; p<0.05 respectively), as well as with Gensini scale points (r=0.56; p<0.05 and r=0.58; p<0.05). In patients involved in quartile 3 and 4, there were found strong correlations between galectin-3 level and Gensini scale points (r=0,73; p<0,05 for 3 quartile r=0.75, p<0.05 for 4 quartile), the number of affected vessels (r=0.70, p<0.05 and r=0.72, p<0.05 respectively), the number of affected segments (r=0.71; p<0.05 and r=0.74; p<0.05 respectively) in patients with AMI and obesity.

Galectin-3 concentrations rising to 23.48 - 41.42 ng/ml, which corresponds to 3-4 quartile, in patients with AMI and obesity was associated with an increasing in the number of affected vessels and segments with high Gensini scores. Thus, in patients with AMI and obesity, the increasing of serum levels of galectin-3 is accompanied by an increasing in the severity of atherosclerotic damage of coronary artery.

The results obtained do not contradict the data of the world medical community. Galectin-3, which is secreted by activated macrophages, is involved in the immune inflammation that underlies the atherosclerotic process [6, 16]. According to Ozturk et al. and Papaspiridonos M. galectin-3 effects associated with amplification of plaque progression by controlling immune inflammation [16, 17] in patients with coronary artery disease, galectin-3 is an independent predictor of coronary atherosclerosis in patients with type 2 diabetes [16].

Conclusions

1. Multi-vessel atherosclerotic lesions were found in 59.3% of patients with AMI and obesity. The most common combination of atherosclerotic lesions in the right coronary artery, the LAD was observed in 25.8% of cases, along with the high incidence of hemodynamically significant stenoses.

2. In most cases, the vascular accident occurred in LAD and RCA (57.1 and 28.6% respectively). In patients with AMI in the context of concomitant abdominal obesity, the overwhelming number of occlusions (60.7%) was found in the proximal segments of the arteries.

3. The obtained data indicate that galectin-3 can be considered as a marker of atherosclerotic process in patients with AMI and obesity due to association with the severity of atherosclerotic damage of coronary arteries.

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**Summary**

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Materials and methods. The study involved 31 patients with AMI and concomitant obesity at the age of 58.42 ± 3.27 years who were treated in the infarction department of the Kharkiv City Clinical Hospital №27. This cohort of patients was performed angiography of the coronary arteries with the subsequent stenting of the infarction-dependent coronary artery within 12 hours from the onset of pain syndrome.

Results. The most common combination of atherosclerotic lesions in the right coronary artery, the LAD was observed in 25.8% of cases, along with the high incidence of hemodynamically significant stenoses. In patients with AMI in the context of concomitant abdominal obesity, the overwhelming number of occlusions (60.7%) was found in the proximal segments of the LAD and RCA arteries. Galectin-3 concentrations rising to 23.48 - 41.42 ng / ml, which corresponds to 3-4 quartile, in patients with AMI and obesity was associated with an increasing in the number of affected vessels and segments with high Gensini scores.

Conclusion. Multi-vessel atherosclerotic lesions were found in 59.3% of patients with AMI and obesity. The obtained data indicate that galectin-3 can be considered as a marker of atherosclerotic process in patients with AMI and obesity due to association with the severity of atherosclerotic damage of coronary arteries.