Determinantion of the temporary disability duration in patients with acute myocardial infarction depending on the body mass index

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Prolonged temporary disability in patients with acute myocardial infarction (AMI) is more common in the presence of concomitant abnormalities. Adipokine C1q/TNF-related protein 3 (CTRP-3) is produced by adipose tissue and exhibits anti-inflammatory and cardioprotective properties. The course and prognosis of AMI depend on the presence of comorbid disorders and hence are objects of scientific interest.

Aim. To identify risk factors affecting the temporary disability duration in AMI patients depending on body mass index (BMI).

Materials and methods. The study involved 189 patients with ST-segment elevation AMI who were divided into 3 groups depending on BMI. The first group included 60 patients with AMI and normal BMI, the second group comprised 68 patients with AMI and excess body weight (EBW) and the third group was composed of 61 AMI patients with obesity. CTRP-3 was determined by enzyme-linked immunosorbent assay. Statistical data were processed using the licensed software package IBM SPSS Statistics (version 27.0). Significance of differences between normally distributed mean values of quantitative variables was assessed by ANOVA with Bonferroni correction for multiple comparisons. The logistic regression method was used to determine the period of temporary disability. The difference was considered significant at a P value < 0.05.

Results. In analyzing the studied indicators, a significant decrease in the concentration of CTRP-3 was found in AMI patients with obesity on the first day compared to AMI patients with normal BMI (P < 0.001), which indicated the effect of obesity on the AMI development. The following indicators were determined to construct a model for predicting the duration of temporary disability, namely CTRP-3 on day 1, glucose on day 1, the presence of permanent atrial fibrillation, early complications of AMI.

Conclusions. The proposed method helped to determine the duration of temporary disability in patients with AMI depending on BMI, which would improve the provision of high-quality diagnostics and treatment of patients by reducing the economic costs of the length of hospital stay.

Key words: adipokine, myocardial infarction, disability, obesity, term.

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Oriгінальні дослідження

Визначення тривалості тимчасової непрацездатності в пацієнтів із гострим інфарктом міокарда залежно від індексу маси тіла

М. Ю. Котелюх

Тривалу тимчасову непрацездатність пацієнта з гострим інфарктом міокарда (ГІМ) спостерігають частіше, якщо в нього є супутня патологія. Адипокін C1q/TNF-зв’язувальний білок 3 (CTRP-3) продукується жировою тканиною, має протизапальну, кардіопротекторну дії. Перебіг і прогноз ГІМ залежать від наявності коморбідної патології, актуалізуючи дослідження в цьому напрямі.

Мета роботи – визначити чинники ризику, що впливають на тривалість тимчасової непрацездатності пацієнтів із ГІМ, залежно від індексу маси тіла (ІМТ).

Матеріали та методи. У дослідженні включали 189 хворих із ГІМ і різним ІМТ. Пацієнтів із ГІМ та елевацією сегмента ST залучали до 3 груп: 60 осіб з ГІМ і нормальним ІМТ, 68 осіб із ГІМ і надлишковою масою тіла, 61 пацієнт із ГІМ та ожирінням. CTRP-3 визначали імуноферментним методом. Статистичне опрацювання даних виконано за допомогою ліцензійного пакета програм IBM SPSS Statistics (версія 27.0). Вірогідність різниць середніх при множинних порівняннях для кількісних ознак із нормальним розподілом із застосуванням тесту Бонферроні оцінювали за допомогою однофакторного дисперсійного аналізу. Для визначення терміну тимчасової непрацездатності використовували метод логістичної регресії. Різницю вважали вірогідною при р < 0,05.

Результати. В результаті аналізу показників встановили вірогідне зменшення концентрації CTRP-3 на 1 добу в пацієнтів із ГІМ та ожирінням порівняно з хворими із ГІМ і нормальним ІМТ (р < 0,001). Це свідчить про вплив ожиріння на розвиток ГІМ. Для побудови моделі прогнозування тривалості тимчасової непрацездатності визначили такі показники: CTRP-3 на 1 добу, глюкоза на 1 добу, наявність постійної форми фібриляції передсердь, ранні ускладнення ГІМ.

Висновки. Запропонований спосіб дав змогу визначити тривалість тимчасової непрацездатності в пацієнтів із ГІМ залежно від індексу маси тіла. Це сприятиме поліпшенню діагностики та лікування пацієнтів шляхом зменшення економічних витрат на перебування в лікарні.

Оригінальні дослідження

Определение продолжительности временной нетрудоспособности у пациентов с острым инфарктом миокарда в зависимости от индекса массы тела

М. Ю. Котелюх

Длительную временную нетрудоспособность пациента с острым инфарктом миокарда (ОИМ) отмечают чаще при наличии у него сопутствующей патологии. Адипокин C1q/TNF-ассоциированный белок 3 (CTRP-3) продуцируется жировой тканью,
Актуальность использования ожирения как нозологического состояния в медицине сегодня. Распространенность ожирения среди населения и его социальные и экономическіе последствия. Важность выявления факторов риска, влияющих на продолжительность временной нетрудоспособности пациентов с ОИМ, в зависимости от индекса массы тела (ИМТ).

Цель работы — определить факторы риска, влияющие на продолжительность временной нетрудоспособности пациентов с ОИМ, в зависимости от индекса массы тела (ИМТ).

Материалы и методы. В исследование включили 189 больных ОИМ с различным ИМТ. Пациентов с ОИМ и элевацией сегмента ST в зависимости от ИМТ поделили на 3 группы: в первую вошли 60 больных с ОИМ и нормальным ИМТ, во вторую — 68 человек с ОИМ с избыточной массой тела, в третью — 61 пациент с ОИМ и ожирением. CTRP-3 определяли иммуноферментным методом.

Статистическую обработку данных осуществили с помощью лицензионного пакета программ IBM SPSS Statistics (version 27.0). Достоверность разницы средних при множественных сравнениях для количественных признаков с нормальным распределением с применением теста Бонферрони оценивали с помощью однофакторного дисперсионного анализа.

Результаты. В результате анализа показателей установили достоверное уменьшение концентрации CTRP-3 на 1 сутки у пациентов с ОИМ и ожирением по сравнению с больными ОИМ и нормальным ИМТ (р < 0,001). Это свидетельствует о влиянии ожирения на развитие ОИМ. Для построения модели прогнозирования продолжительности временной нетрудоспособности определили такие показатели: CTRP-3 на 1 сутки, глюкоза на 1 сутки, наличие постоянной формы фибрилляции предсердий, раньше осложнений ОИМ.

Выводы. Предложенный способ позволил определить продолжительность временной нетрудоспособности у пациентов с ОИМ в зависимости от ИМТ. Это будет способствовать улучшению диагностики и лечения пациентов за счёт уменьшения экономических затрат на пребывание в больнице.

Acute myocardial infarction (AMI) with comorbidity is a topical issue in practical medicine today. Complicated course of AMI is observed more often in the presence of concomitant abnormalities. One of these concomitant abnormalities is obesity, which is associated with the development of AMI [1]. According to G. Velazquez et al. [2], obese patients were more likely to develop inpatient mortality than those with normal body mass index (BMI), and the use of percutaneous coronary intervention improved the course of AMI in obese patients. According to E. Joyce et al. studies [3], adverse left ventricular (LV) and impaired LV deformation were found in patients with ST-segment elevation myocardial infarction (STEMI) and obesity compared with AMI patients and normal BMI. In our opinion, the length of hospital stay is an important indicator of the hospital resource effectiveness, and AMI-related complications in patients are the reasons for longer hospital stays.

Adipokine C1q/TNF-related protein 3 (CTRP-3 or carotenein) has been shown to be involved in carbohydrate and lipid metabolism in obesity [4,5]. CTRP-3 exhibits anti-inflammatory and cardioprotective properties through signaling pathways, attenuates pathological remodeling of the heart after AMI, reduces cardiac dimensions and cardiomyocyte apoptosis, decreases interstitial fibrosis, improves survival rate, and restores the heart function [6].

Zhang C. L. et al. [7] found that CTRP-3 can inhibit cardiac fibrosis and promote mitochondrial biogenesis and bioenergetics in cardiomyocytes. However, the use of CTRP-3 as a factor influencing the length of hospital stay in AMI patients depending on BMI has not been studied to date and therefore is an object of scientific interest.

In our view, the proper use of hospital resources is important for controlling economic costs. According to S. Rehman et al. [8], patients with cardiogenic shock, higher lipid levels, and thyroid disease were more likely to be correlated with longer hospital stays. Improved funding for the diagnosis and treatment of patients might be determined by a decrease in the length of hospital stay. It is essential to identify a complex of risk factors associated with prolonged hospital stays among AMI patients of working age depending on BMI.

**Materials and methods**

In this study we examined 189 subjects with ST-segment elevation AMI depending on BMI, admitted to the SI “L. T. Malay National Institute of Therapy of the National Academy of Medical Sciences of Ukraine” and Kharkiv Clinical Hospital on Railway Transport No. 1, a branch of the Health Care Center of the Ukrainian Railways Public Joint-Stock Company. The study was conducted from 01 September 2018 to 31 December 2020.

Patients with ST-segment elevation AMI were divided into 3 groups depending on BMI. Group 1 included 60 AMI patients with normal BMI, Group 2 involved 68 AMI patients with excess body weight (EBW) and Group 3 was composed of 61 AMI patients with obesity.

Exclusion criteria were diabetes mellitus type 1 and 2, autoimmune diseases, connective tissue diseases, SARS-CoV-2, pituitary and hypothalamic diseases, thyroid disease, the presence of symptomatic hypertension, cancer, chronic obstructive pulmonary disease, heart valve diseases, congestive heart failure IV FC AMI, severe liver and kidney dysfunction, severe anemia.

The author followed all the European Society of Cardiology 2017 guidelines for the diagnosis and management of patients with ST-segment elevation AMI [9]. The diagnosis of permanent atrial fibrillation (it is considered that there is no possibility to restore sinus rhythm for a long time period) was determined according to European recommendations [10]. Early complications included at least one of the parameters: acute LV failure (ALVF) according to Killip classes.
1, 2, 3, 4 within 1–14 days, 2\textsuperscript{nd}–3\textsuperscript{rd} degree atrioventricular (AV) block within 1–14 days, recurrent AMI within 1–14 days. All the patients underwent stenting of the affected coronary artery and subsequently were given standard therapeutic agents. Laboratory parameters were measured in the Biochemical Central Research Laboratory of Kharkiv National Medical University. Serum was collected in 1–2 days following admission.

Serum concentration of CTRP-3 was identified by enzyme-linked immunosorbent assay using Labline-90 analyzer (Austria, No. 2910–2037) and commercial test systems “Human CTRP3” manufactured by AviScora Biotechnology Inc, Santa Clara, USA according to the instructions supplied with a kit. The mean value and reference range for CTRP-3 were set at 325.97 (274.59–399.96) ng/ml. Fasting blood glucose level was measured using glucose oxidase method. Total cholesterol (TC) and high-density lipoprotein cholesterol (HDLC) were determined by peroxidase method using a Human Cholesterol LiquiColor test kit (Germany). The level of triglycerides (TG) was determined by enzymatic colorimetric method using a set of reagents “Triglycerides GPO” produced by “Human” company (Germany). The atherogenic factor (AF) was calculated by the standard A. M. Klimov formula: (TC – HDLC) / HDLC. The level of very low-density lipoprotein cholesterol (VLDLC) was estimated by W. T. Friedewald equation: TG/2.2 and low-density lipoprotein cholesterol (LDLC): TC – (HDLC + VLDLC). All quantitative indicators were checked for normal distribution with the Kolmogorov–Smirnov test. Statistics (version 27.0) (IBM Inc., USA, license No. 60x31) was used for paired comparison.

The χ\textsuperscript{2} test with Yates’s correction was used to compare nominal variables depending on the group size. Significance of differences between normally distributed mean values of quantitative variables was assessed by ANOVA with Bonferroni correction for multiple comparisons. Logistic regression method was used to determine the temporary disability period. The difference was considered statistically significant at a value of P < 0.05.

**Table 1. Overall characteristics of the studied groups, M ± SD, n (%)**

<table>
<thead>
<tr>
<th>Parameters, units of measure</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58.42 ± 8.24</td>
<td>60.03 ± 6.61</td>
<td>57.93 ± 8.62</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>5 (8.33)</td>
<td>11 (16.18)</td>
<td>18 (29.51)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>55 (91.67)</td>
<td>57 (83.82)</td>
<td>43 (70.49)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>WC/TC ratio</td>
<td>0.76 ± 0.06</td>
<td>0.84 ± 0.05</td>
<td>1.21 ± 0.34</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>23.52 ± 1.25</td>
<td>27.06 ± 1.29</td>
<td>23.77 ± 2.47</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>7.12 ± 0.65</td>
<td>6.76 ± 0.62</td>
<td>6.50 ± 0.84</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>CTRP-3, ng/ml</td>
<td>272.31 ± 56.98</td>
<td>235.69 ± 49.49</td>
<td>234.03 ± 43.17</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Early complications of AMI</td>
<td>18 (30.00)</td>
<td>19 (27.94)</td>
<td>19 (31.15)</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

Results

BMI-dependent characteristics of AMI patients, including demographics and laboratory parameters, are shown in Table 1.

Among AMI patients (n = 189) in the study, 82.01 % were male and 17.99 % were female. The mean age of all patients was 58.79 ± 0.99 years. All groups did not differ in glucose level, the presence of permanent atrial fibrillation or early complications of AMI (P > 0.05). The total number of early complications of AMI among all patients was 29.63 %. Out of the total number of patients (n = 189) who participated in the study, 68.25 % of subjects were with excess body weight (Groups 2 and 3), and 31.75 % of AMI patients had normal BMI (group 1). CTRP-3 levels in Group 2 were reduced by 13.45 % and in Group 3 – by 23.86 % compared to Group 1 (P < 0.001). Group 3 patients were found to have significantly increased parameters of lipid metabolism: VLDLC by 28.77 % (P < 0.05), TG by 26.71 % (P < 0.05), AF by 17.43 % (P < 0.05) and decreased HDLC by 9.38 % (P < 0.05) compared to Group 1 (Table 2). There was no significant difference in the values of lipid metabolism between Groups 1 and 2. In Group 1, a direct correlation was revealed between CTRP-3 and TC (r = 0.413, P = 0.001), LDLC (r = 0.329, P = 0.01), TG (r = 0.363, P < 0.01), AF (r = 0.336, P < 0.01). An inverse correlation was found between CTRP-3 and lipid metabolism indicators in Group 3: between CTRP-3 and TC (r = -0.426, P < 0.001), LDLC (r = -0.405, P < 0.01), TG (r = -0.314, P < 0.01).

The data obtained from 189 AMI patients depending on BMI were included to build the model. The method was as follows: a patient was diagnosed with early complications (ALVF according to Killip classes 1, 2, 3, 4 within 1–14 days, 2\textsuperscript{nd}–3\textsuperscript{rd} degree AV block within 1–14 days, recurrent AMI...
Table 2. Lipid metabolism indicators in AMI patients depending on BMI, M ± SD

<table>
<thead>
<tr>
<th>Parameters, units of measure</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC, mmol/l</td>
<td>5.17 ± 1.21</td>
<td>5.43 ± 1.13</td>
<td>5.39 ± 1.40</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>VLDLC, mmol/l</td>
<td>0.73 ± 0.50</td>
<td>0.79 ± 0.45</td>
<td>0.94 ± 0.38</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>LDLC, mmol/l</td>
<td>3.20 ± 0.94</td>
<td>3.55 ± 1.08</td>
<td>3.32 ± 1.30</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>TG, mmol/l</td>
<td>1.61 ± 1.13</td>
<td>1.73 ± 0.91</td>
<td>2.04 ± 0.83</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>HDLC, mmol/l</td>
<td>1.28 ± 0.31</td>
<td>1.23 ± 0.53</td>
<td>1.16 ± 0.24</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>AF</td>
<td>3.27 ± 1.20</td>
<td>3.84 ± 1.47</td>
<td>3.84 ± 1.65</td>
<td>P &gt; 0.05</td>
</tr>
</tbody>
</table>

Within 1–14 days, glucose level on day 1, the presence of permanent atrial fibrillation, cartonectin content on day 1. The number of disability days in the patient was calculated according to the developed formula:

\[
D = 0.144 \times X_1 - 3.056 \times X_3 + 5.288 \times X_4 - 0.006 \times X_1 + 12.212
\]

where D is the number of disability days;

- \(X_1\) – blood glucose on day 1, mmol/l;
- \(X_2\) – permanent atrial fibrillation (1 – absent; 2 – present);
- \(X_3\) – early complications of AMI (1 – absent; 2 – present);
- \(X_4\) – cartonectin on day 1, ng/ml.

The probability of the disability period duration was determined by the method of logistic regression and by the conversion log using the formula:

\[
P = \frac{1}{1 + e^{-(30.37 – 15.5)}}
\]

where \(P\) – the probability of prolonged disability;

- \(e\) – the basis of the natural logarithm (\(e = 2.718\));
- \(D\) – the number of disability days.

The mean disability period in hospital patients was 15.5 days and if values ranged from 0.5 to 0.8, the probability was estimated as average, if more than 0.8 – as high, if less than 0.5 – as low.

All variables and the constants of the proposed model met the considered statistical significance at the level of \(P < 0.05\). The mean relative error in calculating the number of work disability days was only 1.1 %.

Clinical example 1. A 57-year-old patient was hospitalized to the cardiology department with CHD. The patient was diagnosed with ST-segment elevation AMI (05.12.2019). According to medical history, the patient's risk profile included obesity. In the course of the treatment, the patient was not found to have recurrent chest pain, dizziness, resting or exertional breathlessness, arrhythmia and conduction disorders. On examination, his BMI was 25.7 kg/m². Based on laboratory data, the glucose level on day 1 was 5.11 mmol/l, the content of cartonectin on day 1 was 301.2 ng/ml. The patient showed no signs of atrial fibrillation on electrocardiography (ECG). Calculation according to the proposed formula was as follows:

\[
D = 0.144 \times 11.6 – 3.056 \times 1 + 5.288 \times 2 – 0.006 \times 187.58 + 12.212 = 20.27
\]

and the probable duration of the patient’s disability was determined as:

\[
P = \frac{1}{1 + e^{-(30.37 – 15.5)}} = 0.99.
\]

Therefore, the probability of the hospital length of stay for the patient was defined as very high, the estimated disability period in the hospital was 20 days. Therefore, the patient was discharged on day 20.

Clinical example 2. A 63-year-old patient was hospitalized to the cardiology department with CHD. The patient was diagnosed with ST-segment elevation (23.05.2019). The patient had a history of obesity over the last 5 years. In the treatment course, the patient presented with resting or exertional breathlessness. He was diagnosed with ALVF: pulmonary edema. BMI of 30.8 kg/m² was determined on examination, and grade 1 obesity was diagnosed. Based on the laboratory data, the glucose level on day 1 was 11.6 mmol/l, the cartonectin content on day 1 was 187.58 ng/ml. The patient showed no signs of atrial fibrillation on ECG. Calculation according to the proposed formula was as follows:

\[
D = 0.144 \times 11.6 – 3.056 \times 1 + 5.288 \times 2 – 0.006 \times 187.58 + 12.212 = 20.27
\]

and the probable duration of the patient’s disability was determined as:

\[
P = \frac{1}{1 + e^{-(30.37 – 15.5)}} = 0.11.
\]

Thus, the length of stay probability for the patient was defined as insignificant, the determined disability period in the hospital was 13 days. Therefore, the patient was discharged on day 12.

Discussion

In our study, the risk factors for long-term temporary disability in AMI patients depending on BMI were the content of cartonectin on day 1, the presence of permanent atrial fibrillation, glucose level on day 1, at least one detected early complications of AMI. The use of glucose in the model can be explained by the fact that CTRP-3 was associated with carbohydrate metabolism. According to our study, cartonectin was associated with TC, LDLC, and TG in AMI patients with obesity.

Chen L. et al. [13] identified that CTRP-3 rates were significantly decreased in subjects with persistent atrial fibrillation compared with paroxysmal atrial fibrillation. In our opinion, a decrease in the concentration of cartonectin leads to a deterioration in the ability to protect the heart and thus may affect the process of LV myocardial remodeling in AMI patients with different BMI values. According to studies
of Yildirim A. et al. [14], decreased CTRP-3 levels were associated with the presence of ventricular tachycardia in patients with heart failure and low ejection fraction. Jang S. et al. [15] determined that a longer stay was an independent prognostic factor for the increase in overall costs for both patients with non-ST elevation myocardial infarction and STEMI. Wasfy J. H. et al. [16] identified that the predictors of prolonged hospital stay were as follows: older age, heart failure on hospital admission, higher heart rate on admission, systolic blood pressure <150 mm Hg, cardiogenic shock, diabetes, decreased glomerular filtration rate and hemoglobin. Scientists S. Vallabhajosyula et al. [17] found that longer hospital stays, higher hospital costs, and fewer home discharges were associated with the development of LV aneurysms in patients with AMI.

According to C. Baechlia et al. [18], not only older age prolonged hospital stays compared to younger age, but hospital stays also depended on the presence of comorbidity abnormalities.

Conclusions
1. The study showed the low CTRP-3 content in AMI patients depending on BMI indicating an imbalance in the adipokine system and the lesser impact of CTRP-3 on the inflammatory process in AMI.
2. Patients with AMI were found to have positive correlations between TC, LDL-C, TG, AF. In contrast, AMI patients with obesity were shown to have inverse correlations between CTRP-3 and lipid metabolism, namely TC, LDL-C, TG.
3. The study provided a possibility to elaborate the mathematical model for determining the temporary disability duration in AMI patients depending on BMI, which included the following indicators: glucose, cartecinone on day 1 day, the presence of a permanent atrial fibrillation and early complications of AMI.

Perspectives for further research. It is planned to study the effect of CTRP-3 on the condition of coronary arteries in AMI patients depending on BMI. We plan to study the effect of СTRP-3 on the condition of coronary arteries in AMI patients depending on BMI indicating an imbalance in the mathematical model for determining the temporary disability duration in AMI patients depending on BMI, which included the following indicators: glucose, cartecinone on day 1 day, the presence of a permanent atrial fibrillation and early complications of AMI.

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Conflicts of interest: author has no conflict of interest to declare.

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