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INFLAMMATION SYNDROME WITH AUTOIMMUNE COMPONENT IN THE PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: QUANTUM GENETIC ALGORITHM, NEURONET

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The purpose of the study was optimizing the diagnosis of the inflammatory syndrome with an autoimmune component in patients with acute myocardial infarction using a quantum genetic algorithm and graph neural networks. There were 47 patients observed with acute myocardial infarction, and among them, 35 experienced complications. The diagnostic criteria of the inflammatory syndrome with an autoimmune component include elevated level of ratio of chaperone 60 autoantibodies to interleukin-10 more than 4.99 conditional units, ratio of chaperone 60 autoantibodies to C-reactive protein more than 4.2 conventional units, ratio of C-reactive protein to interleukin-10 is less than 0.2 conventional units. This syndrome was present in 33 (70.2 %) out of 47 myocardial infarction patients (p=0.01 by the Chi-Square test). It was presented on visual programming language "Dragon". Quantum genetic algorithm, graph neural networks using for making decisions for an inflammation syndrome with autoimmune component diagnosis presented in this investigation.

Key words: Graph neural networks, inflammation syndrome with autoimmune component, acute myocardial infarction, diagnosis.

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СИНДРОМ ЗАПАЛЕННЯ З АУТОІМУННИМ КОМПОНЕНТОМ У ХВОРИХ З ГОСТРИМ ІНФАРКТОМ МІОКАРДА: КВАНТОВИЙ ГЕНЕТИЧНИЙ АЛГОРИТМ, НЕЙРОМЕРЕЖА

Мета дослідження полягала в оптимізації діагностики запального синдрому із автоімунною складовою у пацієнтів із гострим інфарктом міокарда за допомогою квантового генетичного алгоритму та графових нейронних мереж. Спостерігали за 47 пацієнтами із гострим інфарктом міокарда, у 35 з яких виникли ускладнення. Діагностичні критерії запального синдрому із аутоімунним компонентом включають підвищений рівень співвідношення аутоантитіл до шаперону 60 до інтерлейкіну-10 більше 4,99 умовних одиниць, співвідношення антитіл до шаперону 60 до С-реактивного білка більше 4,2 умовних одиниць, співвідношення С-реактивного білка до інтерлейкіну-10 менше 0,2 умовних одиниць. Цей синдром був виявлений у 33 (70,2 %) з 47 пацієнтів із інфарктом міокарда (p=0,01 за тестом Хі-квадрат). Результати презентовані мовою візуального програмування "Dragon". Квантовий генетичний алгоритм та графові нейронні мережі використовувалися для прийняття рішень у діагностиці запального синдрому із автоімунною складовою в цьому дослідженні.

Ключові слова: графові нейронні мережі, синдром запалення з аутоімунним компонентом, гострий інфаркт міокарда, діагностика.

The study is a fragment of the research project "Improving methods of diagnosis, treatment and prevention of drug-induced lesions of internal organs", state registration No. 0121U113862.

The development of acute myocardial infarction (AMI) leads to the emergence of a systemic and local inflammatory response, activation of acute-phase proteins, including components of the complement system, C-reactive protein, α-antitrypsin, kallikrein, and kinins [9, 11, 13]. Systemic modulation manifests in the development of fever, pain, leukocytosis, bone marrow stimulation, the appearance of prostaglandins, interferon, and acute-phase proteins. Studies have revealed the role of pro-inflammatory and anti-inflammatory cytokines such as interleukins: IL-6, IL-8, IL-1b, IL-10, and tumor necrosis factor in the course of cardiovascular diseases. It's worth noting that the peak concentration of CRP correlates with the maximum increase in IL-6 content [2, 10, 15]. In the early stage of inflammation, CRP is part of the mechanism of macrophage activation, inducing chemotaxis and superoxide production at the same time, it is noted that C-reactive protein has the potential to inhibit chemotaxis, degranulation of healthy cells, phagocytosis, and has an immunosuppressive effect [11].

Cellular and humoral immunity to heat shock protein 60 is an initiating mechanism in the early stages of atherosclerosis. If arterial endothelial cells are exposed to classical risk factors of atherosclerosis, this leads to the expression of hsp60, which can become a target for the cross-reaction of the antimicrobial immunity against this protein [6].

The purpose of the study was to optimize the diagnosis of the inflammatory syndrome with an autoimmune component in patients with acute myocardial infarction using a quantum genetic algorithm and graph neural networks.

Materials and methods. According to the data from intelligent statistical analysis, the results of the study of 47 patients diagnosed with acute myocardial infarction within the first day, 35 of them with complication, allowed for the determination of diagnostic criteria for the inflammatory syndrome with an autoimmune component. The research is based on the results of research conducted at the Cardiology Department of the Poltava Regional Clinical Medical Cardiovascular Center during the years 2006-2008.

The diagnosis of AMI was determined in accordance with the standards of care for cardiac patients, as per the order No. 436 of the Ministry of Health of Ukraine dated July 3, 2006. Out of the 47 individuals examined, 37 (79 %) were diagnosed with ST-segment elevation myocardial infarction (STEMI) with deep Q-wave or QS complex, and 10 (21 %) with non-ST-segment elevation myocardial infarction (NSTEMI). Complicated courses of AMI were observed in 35 (74.5 %) out of 47 cases. 16 (34 %) of the 47 patients experienced recurrent AMI. In 9 (19.1 %) of the 47 patients, a recurrence of myocardial infarction occurred. Additionally, 42 (89.4 %) of the examined individuals suffered from arterial hypertension, stage III. In the study, 35 out of 47 patients (74.5 %) reported a history of angina pectoris. Among the participants, 13 patients (27.7 %) were identified with Stage I heart failure according to M.D. Strazhesko, V.H. Vasilenko, and Class II functional status according to NYHA, while 33 patients (70.2 %) were classified as Class II A, and 1 patient (2.1 %) as Class II B, according to NYHA's Class III functional status.

Complications of AMI included events occurring within the first 12 hours or the initial day: acute heart failure according to the T. Killip-J. Kimbal classification (1969), grouped ventricular and supraventricular extrasystoles, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, acute aneurysm, and recurrent myocardial infarction.

Inclusion criteria for the study were the presence of AMI within the first twelve hours of onset and signed informed consent to participate in the research. Exclusion criteria included Class III chronic heart failure, decompensated comorbidities, acute cerebrovascular events, oncological diseases, and acute inflammatory conditions.

The mean age of AMI patients was 70.32± 6.71 (M ± SEM). Complicated AMI were present in 35 (74.5 %) out of 47 individuals, and 16 (34 %) out of 47 patients had recurrent AMI.

The levels of interleukin-10, C-reactive protein, and autoantibodies to heat shock protein 60 were investigated using the enzyme-linked immunosorbent assay (ELISA) method. The following reagent kits were used: ProCon IL-10 for interleukin-10, hsCRP ELISA for C-reactive protein, and Anti-Human Hsp60 Standard ELISA Kit for autoantibodies to heat shock protein 60. The determination of systemic inflammation indicators was conducted at the Research Institute of Genetic and Immunological Foundations of Pathology and Pharmacogenetics at Poltava State Medical University.

The research data was statistically processed using the IBM SPSS Statistics 22.00 program and SPSS for Windows Release 13.00. The following statistical measures were computed: median (Me), lower and upper quartiles (Q). The statistical analysis of the obtained results included the non-parametric Mann-Whitney U (MW) test for comparing variabilities of two independent samples. The normality of the distribution of variations was assessed using the Shapiro–Wilks test (W test). The Chi-square test was employed to evaluate discrepancies in categorical variables. A difference between compared values was considered significant at $p < 0.05$. We used the dynamic and multi-paradigm programming language Dragon for Cross-platform (multi-platform) operating systems.

Results of the study and their discussion. In patients with uncomplicated AMI, a higher level of IL-10 is observed compared to those who experienced complications. Conversely, a reverse pattern is observed in the ratio of chaperone autoantibodies to the interleukin 10 (Table 1).

Table 1

Markers of cytokine exchange and changes in the level of autoantibodies to heat shock protein 60 in patients with acute myocardial infarction with complicated and uncomplicated course

Parameters, units of measurement	Patients with AMI depending on the course of the disease:	
	complicated (n=35)	uncomplicated (n=12)
Interleukin-10 (IL-10), pg/mL	6.0 (3.00–54.50) non-parametric according to Shapiro-Wilk Psw=0.0001 PMW=0.001	45.65 (10.92–134.67) non-parametric according to Shapiro-Wilk Psw=0.016
The ratio of chaperone autoantibodies to interleukin-10, arbitrary units, u.a.	5.7 (0.21–5.46) non-parametric according to Shapiro-Wilk Psw=0.0001 PMW=0.008	1.21 (1.78–6.04) non-parametric according to Shapiro-Wilk Psw=0.01
Autoantibodies to heat shock protein 60, ng/mL	62.90 (38.40–112.00) non-parametric according to Shapiro-Wilk Psw=0.032 PMW=0.052	40.55 (28.62–73.65) non-parametric according to Shapiro-Wilk Psw=0.003

Notes: Med – median; Q – lower and upper quartiles; Pmw – difference between groups according to the non-parametric equivalent of the two-sample t-test Student's t-test – Mann-Whitney (MW), Psw – determination of distribution type of variability according to Shapiro-Wilks test.

Comparison of the inflammatory syndrome with an autoimmune component in patients with AMI, both uncomplicated and complicated, allowed us to determine that this syndrome is a risk factor for an unfavorable course. This syndrome was present in 33 (70.2 %) out of 47 myocardial infarction patients (P=0.01 by the Chi-Square test).

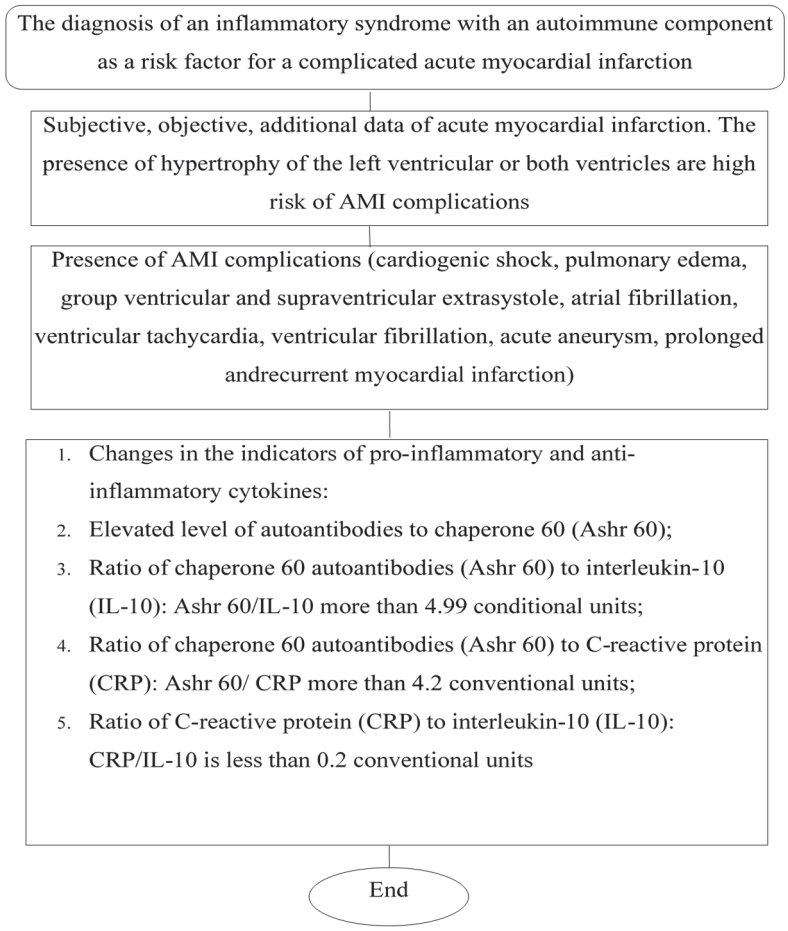

Fig. 1. Diagnosis of an inflammatory syndrome with an autoimmune component as a risk factor for a complicated acute myocardial infarction by visual programming on "Dragon" language.

Changes in the indices of pro-inflammatory and anti-inflammatory cytokines:

– Elevated level of autoantibodies to chaperone 60 (Ashr 60);

– Ratio of chaperone 60 autoantibodies (Ashr 60) to Interleukin-10(IL-10): Ashr 60/IL-10 more than 4.99 conditional units;

– Ratio of chaperone 60 autoantibodies to C-reactive protein more than 4.2 conventional units;

– Ratio of C-reactive protein (CRP)/Interleukin-10 (IL-10) CRP/IL-10 is less than 0.2 conventional units.

The proposed method of diagnosing an inflammatory syndrome with an autoimmune component as a risk factor for a complicated course of an acute myocardial infarction evaluated for sensitivity, specificity, and accuracy.

Diagnostic sensitivity reached 91.4 %, specificity – 91.7 %, index of accuracy or diagnostic efficiency – 96.97 %.

It's known that genetic algorithms, graph neural networks are basic directions to artificial intelligence formation.

The diagnosis of an inflammatory syndrome with an autoimmune component as a risk factor for a complicated AMI presented on visual programming language "Dragon" (Fig. 1).

We used Typical Conceptual Spaces by some principles as information is organized by quality dimensions that are sorted into domains; domains are endowed with a topology or metric; similarity is represented by distance in a conceptual space.

We used our modified domains for analysis of inflammatory syndrome with an autoimmune component as a risk factor for a complicated course of an acute myocardial infarction:

Domain 1. Qualitative characteristics of ECG waves, segments, intervals; echocardiography (The presence of hypertrophy of the left ventricular or both ventricles);

Domain 2. Elevated level of autoantibodies to chaperone 60 - Ashr 60;

Domain 3. Changes in the indicators of pro-inflammatory cytokines (Elevated level of autoantibodies to chaperone 60-Ashr 60 to Interleukin-10 more than 4.99 conditional units;

Domain 4. Changes in the indicators of pro-inflammatory and anti-inflammatory cytokines (Ratio of chaperone 60 autoantibodies to C-reactive protein more than 4.2 conventional units):

Domain 5. Changes in the indicators of pro-inflammatory and anti-inflammatory cytokines (Ratio of C-reactive protein to Interleukin-10 is less than 0.2 conventional units);

The quantum genetic algorithm using for diagnosis of inflammation syndrome with autoimmune component as risk factor of complicated acute myocardial infarction:

|q>□□1|0>□□2|1>

|q1>□□1 (level of autoantibodies to chaperone 60) |0>□□2 (level of C-reactive protein) |1>

|q2>□□1 (level of C-reactive protein) |0> □2 (level of Interleukin-10) |1>

Implementation of our algorithms on visual programming language “Dragon”, using modified domains of Typical Conceptual Spaces, quantum genetic algorithms gave us possibilities to graph neural networks decision-making of diagnosis of inflammation syndrome with autoimmune component as risk factor of complicated AMI (Fig. 2).

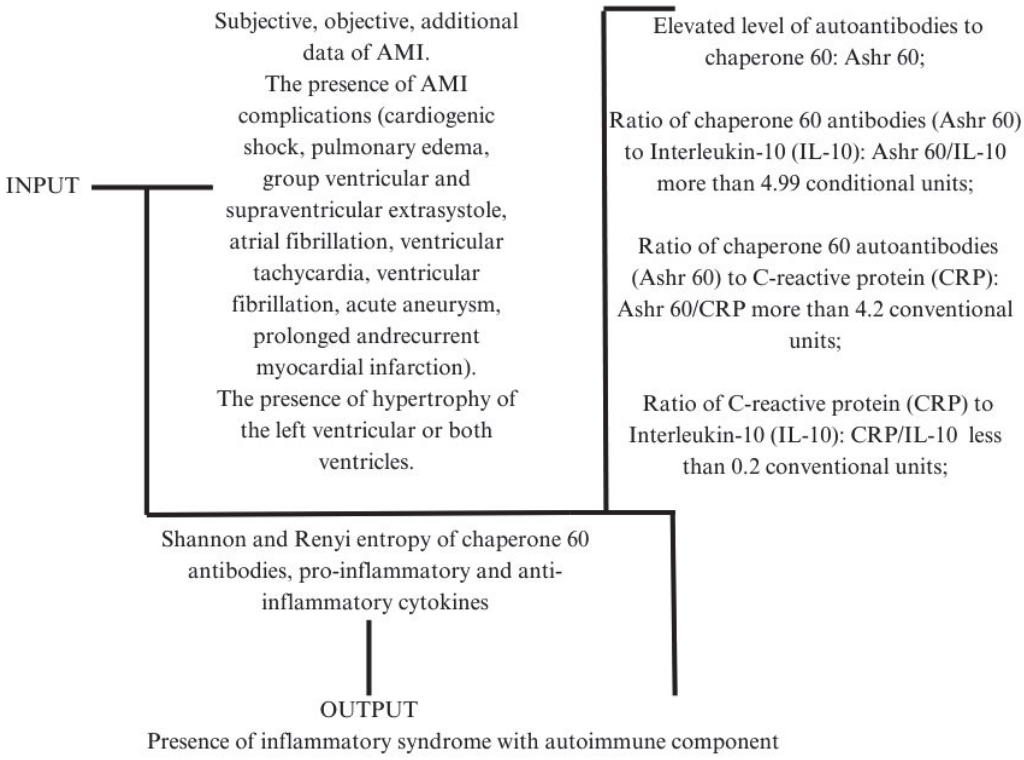

Fig. 2**.** Graph neural network using for making decisions by an inflammation syndrome with autoimmune component.

We used Shannon and Renyi entropy for diagnosis of inflammation syndrome with autoimmune component as risk factor of complicated AMI.

Thus, the diagnosis of the inflammatory syndrome with an autoimmune component in patients with AMI was based on a combination of clinical manifestations of ischemia, necrobiosis, myocardial necrosis, pulmonary edema, cardiogenic shock, life-threatening disruptions in heart rhythm and conduction, the formation of acute left ventricular aneurysm, as well as specific alterations in pro-inflammatory and anti-inflammatory cytokines, and the level of autoantibodies to chaperone 60.

Andreas Mitsis and co-authors (2022) note that elevated levels of key proinflammatory cytokines TNFα, IL-6, and IL-1, as well as adipokines adiponectin, visfatin, and resistin, are associated with high mortality and morbidity. Conversely, there is evidence that anti-inflammatory cytokines and adipokines such as IL-10, omentin-1, and ghrelin can suppress the inflammatory response induced by AMI and are correlated with a better prognosis [8].

A meta-analysis of Chongzhe Yang and co-authors (2021) investigating the correlation between IL-6 and the severity of acute coronary syndrome (ACS) revealed a significant elevation in plasma IL-6 levels among patients in the severe group compared to those in the non-severe group ($p<0.00001$). Moreover, individuals with a history of major adverse cardiovascular events exhibited markedly higher plasma IL-6 levels than those without such events ($p<0.00001$). Thus, IL-6 levels may serve as indicators for predicting adverse cardiovascular events and assessing the severity of ACS [14].

Similarly to our study, researchers note in their investigation that an imbalance between pro-inflammatory and anti-inflammatory cytokines may lead to a worse prognosis in AMI. A promising direction for research remains the development of an algorithm for diagnosing and predicting adverse cardiac events in patients with AMI, as well as the search for new markers for their prognosis.

Principles of conceptual spaces domains, Shannon and Renyi entropy [1, 3, 4, 5], quantum genetic algorithms [7, 12], graph neural networks using for making decisions an inflammation syndrome with autoimmune component as risk factor of complicated myocardial infarction presented in this article.

Additional research is required to identify the optimal combination of biomarkers and assess the prognostic value they could contribute to established prognostic models. These inflammatory and autoimmune markers may serve as viable targets for novel medications aiming to enhance the prognosis of patients with AMI.

Conclusions

1. In order to assess the presence of inflammation syndrome with an autoimmune component in patients with acute myocardial infarction, measurements of C-reactive protein, interleukin-10, chaperone 60 autoantibodies and their ratio are recommended. The diagnosis of the inflammatory syndrome with an autoimmune component in patients with acute myocardial infarction allows for assessing the likelihood of an unfavorable course of AMI.

2. The quantum genetic algorithm, employed for diagnosing inflammation syndrome with an autoimmune component in addition to the primary diagnostic criteria, incorporates the presence of: elevated levels of autoantibodies to chaperone 60 (Ashr 60); elevated levels of autoantibodies to chaperone 60-Ashr 60 to Interleukin-10 exceeding 4.99 conditional units; ratio of chaperone 60 autoantibodies to C-reactive protein more than 4.2 conven-tional units; ratio of C-reactive protein to Interleukin-10 being less than 0.2 conventional units, serving as a risk factor for complicated AMI (p=0.01 by the Chi-Square test).

Perspectives of subsequent scientific research. The obtained results have their further development for timely diagnosis of inflammation syndrome with autoimmune component in patients with acute myocardial infarction using a quantum genetic algorithm and graph neural networks, which will help prevent complications and improve the quality of life for patients.

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