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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

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გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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CONTACT ADDRESS IN TBILISI

GMN Editorial Board
7 Asatiani Street, 4th Floor
Tbilisi, Georgia 0177

Phone: 995 (32) 254-24-91
995 (32) 253-70-58
Fax: 995 (32) 253-70-58

CONTACT ADDRESS IN NEW YORK

NINITEX INTERNATIONAL, INC.
3 PINE DRIVE SOUTH
ROSLYN, NY 11576 U.S.A.

Phone: +1 (917) 327-7732

WEBSITE
www.geomednews.org

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1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

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При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

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2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

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In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

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ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

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5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

НАУКА

ANALYSIS OF POLYMORPHISM OF MATRIX METALLOPROTEINASE-2 ($C^{-1306} \rightarrow T$) AND TISSUE INHIBITORS OF METALLOPROTEINASE-2 ($G^{303} \rightarrow A$) GENES IN PATIENTS WITH ANASTOMOTIC LEAK IN HOLLOW DIGESTIVE ORGANS

[1]Voitiv Y., [2]Usenko O., [3]Dosenko V., [1]Dyadyk O., [2]Dzhemiliev A.

[1]Shupyk National Academy of Postgraduate Educationof the Ministry of Health of Ukraine;
[2]Shalimov National Institute of Surgery and Transplantology, National Academy of Medical Sciences of Ukraine;
[3]Bogomoletz Institute of Physiology, National Academy of Sciences of Ukraine, Kyiv, Ukraine

Despite the improvement of existing techniques and the development of new surgical technologies, the anastomotic leak in the hollow digestive organs is one of the most difficult complications in abdominal surgery. The incidence of such complications, according to various authors, ranges from 2-8.1% in small bowel anastomosis to 3.8-14.6% in operations on the colon [1,2]. Anastomotic leak is accompanied by mortality rate of 14-21.7% [3]; with the development of disseminated peritonitis, abdominal sepsis mortality increases up to 43-82.9% [1,4]. So far, there is no single point of view in the surgical community regarding the causes of anastomotic leak development and surgical tactics in the development of these complications. According to the literature on the subject, among the risk factors for the development of an anastomotic leak are microcirculation disruption in the anastomosis area, tissue regeneration failure, infection, increased intra-intestinal pressure, changes in the rheological properties of blood, homeostatic imbalances, etc. [1]. A separate group of risk factors includes tactical and technical errors in the formation of anastomosis [5].

Although there is no doubt about the role of regenerative processes in the formation of intestinal anastomosis [6,7], scientific publications and research at the current methodological level on this topic are not enough. An in-depth study of the mechanisms of reparative regeneration in the area of the anastomosis and possibilities of regenerative processes stimulation, adequate restoration of morpho-functional characteristics of digestive organs that have been anastomosed is necessary. In domestic and foreign sources, there are almost no publications about the role of undifferentiated dysplasia of the connective tissue (UDCT) in the development of anastomotic leak in hollow digestive organs.

Anastomosis formation is a complex molecular- and cell-mediated process aimed at restoring of the continuity of the hollow digestive organs [7]. It involves both classical processes of inflammation: alteration, exudation, proliferation, and specific reparative processes due to suture technique, suture material, the presence of infection, and other factors [8].

Given the almost unexplored role of genetic predisposition in the development of postoperative complications, namely the failure of anastomotic sutures, we set a goal to study the polymorphism of genes encoding matrix metalloproteinase-2 (MMP-2) and tissue inhibitor of matrix metalloproteinase-2 (TIMP-2). The choice of these genes was not accidental - we were guided by the main known pathophysiological mechanisms involved in the formation of the intestinal anastomosis [7].

Matrix metalloproteinases (MMPs) are a group of enzymes represented by cysteine, serine, aspartyl, and metal-dependent proteinases. They belong to Zn^{2+} - and Ca^{2+}-dependent endopeptidases, which are involved in the remodeling of connective tissue due to the destruction of its organic components at normal pH values. MMPs play a major role in the metabolism of connective tissue proteins. These enzymes are also involved in many physiological (embryonic development, morphogenesis, migration, adhesion, angiogenesis, involution, and tissue remodeling) and pathological (inflammation, malignancy, cardiovascular, pulmonary diseases, arthritis) processes. They are also able to model the activity of growth factors, cytokines, and their receptors. Enzymes from the MMPs group (MMPs -2, -3, -9) affect vascular wall permeability and angiogenesis by regulating the catabolism of extracellular matrix components and cell-matrix interactions [9]. Currently, approximately 30 different MMPs are known, which are divided into 5 groups based on substrate specificity: collagenases; gelatinases; stromelysins; membrane-bound; other matrixins not included in the above groups. The gelatinase subfamily includes 2 enzymes - gelatinase A (MMP-2) and gelatinase B (MMP-9). MMP-2,9 show a high affinity for type IV collagen, so they are sometimes called type IV collagenases. MMP-2 occupy a central position in the regulating of the balance between the processes of synthesis and proteolysis in the extracellular matrix, affect the implementation of physiological processes and pathological changes in the body [9].

The main regulators of matrix metalloproteinases are tissue inhibitors of metalloproteinases - TIMPs (TIMP-1, TIMP-2, TIMP-3, TIMP-4). All 4 groups of TIMPs can inhibit the proteolysis of latent forms of MMP and inhibit the active forms of MMP, but TIMP-1 is more active against MMP-9, and TIMP-2 shows specificity for MMP-2 [10].

Recently these enzymes, namely their expression, polymorphism of the genes that encode them, have been actively studied as diagnostic and prognostic factors in oncological diseases [11,12,13], cardiovascular pathology [14,15], ophthalmology [16], etc.

At the same time, information on the role of MMPs in the development of anastomotic leak in hollow digestive organs is almost absent. During the analysis of the literature, we found a small number of publications on the study of MMP expression in the colorectal anastomoses leak [17-19], postoperative peritonitis [20,21].

However, we have not found publications on the study of genetic polymorphism of matrix metalloproteinases and their regulators in terms of the development of anastomotic leak.

The aim - to analyze the frequency of polymorphic variants of genes MMP-2 ($C^{-1306} \rightarrow T$) and TIMP-2 ($G^{303} \rightarrow A$) in patients with anastomotic leak in hollow digestive organs.

Material and methods. A retro- and prospective trial was based on data on 61 patients, who were treated at the Shalimov National Institute of Surgery and Transplantology. 17 of 61 patients (experimental group 2) suffered anastomotic leak in hollow digestive organs, 44 of 61 patients (experimental group 1) had phenotypic signs of UDCT. For the assessment of genetic polymorphism in the population, 80 practically healthy people

have been examined (control group), who were matched by gender and age with experimental groups. Of the special laboratory tests, we have measured serum procalcitonin and C-reactive protein. For the assessment of connective tissue, we analyzed free hydroxyproline in the serum and urinary glycosaminoglycans. UDCT has been diagnosed with a proven technique (Ukrainian patent for utility model №120158 UA). The stage of dysplasia was evaluated using the original clinical screening scale, which was based on the table of the severity criteria of connective tissue dysplasia made by T.Y. Smolnova (2003) [22].

Genetic studies were performed in the laboratory of the Department of General and Molecular Pathophysiology at the Bogomoletz Institute of Physiology NAS of Ukraine. The collection of the buccal epithelium was performed using buccal brushes with the upcoming freezing of the samples at the temperature of -20 ° C. DNA for the genotyping was extracted from the samples using Diatom™ Prep 200 (Isogen Laboratory, RF) following the manufacturer's protocol.

The following polymorphisms were studied by real-time PCR: $C^{-1306} \rightarrow T$ (MMP2), rs243865 and $G^{303} \rightarrow A$ (TIMP2), rs9900972. Amplification reactions were performed using the Fast Real-time PCR System (Applied Biosystems, USA) in a final reaction volume of 20 µl containing 2X TaqMan Universal Master Mix (Applied Biosystems, USA), assay C_1792560_10 and template DNA. Amplification of gene fragments consisted of a denaturation step at 95° C for 20 s, followed by 40 cycles of amplification at 95° C for 3 s and 60° C for 30 sec. Data analysis was performed with 7500 Fast Real-Time PCR Software (Applied Biosystems, Foster City, USA).

The main part of the statistical analysis was performed using the program «Statistica 7.0» (SPSS) and Excel 2000. Nominal data were presented in the form of quantitative and percentage values. The significance of differences in mean values in groups with different genotypes was determined using the method of one-way analysis of variance (URL: http://www.dgmp.kyiv.ua/index.php/snip-ka). The correspondence of genotype distribution was checked using the Hardy-Weinberg test. Pearson's $\chi 2$ test was used to compare the distribution of genotypes in the experimental and control groups.

Results and discussion. To identify the possible association of polymorphic variants of the MMP-2 ($C^{-1306} \rightarrow T$) and TIMP2 ($G^{303} \rightarrow A$) genes with the risk of anastomotic leak, we performed a one-way analysis of variance of the frequency of genotypes in the studied groups of patients (Table 1).

In the analysis of models of inheritance of the MMP2 gene ($C^{-1306} \rightarrow T$), namely codominant, dominant, recessive, supradominant and additive in the control group (n = 80) and the experimental group 1 with phenotypic signs of UDCT (n = 44), it was found that the distribution of genotypes corresponds to the Hardy-Weinberg law (p> 0.05). Using the $\chi 2$ test with 2 degrees of freedom, we were not able to detect statistically significant differences in the distribution of genotypes in the group of sick people and the group of practically healthy people (p>0.05).

Having analyzed all inheritance models, we selected the best model with the lowest Akaike Information Criterion. Such a model turned out to be a recessive model, for which the table shows the values of the odds ratio, statistical significance, as well as the Akaike Information Criterion (AIC) (Table 2).

Table 1. The distribution of polymorphic variants of genes MMP-2 ($C^{-1306} \rightarrow T$), rs243865 and TIMP-2 ($G^{303} \rightarrow A$), rs9900972 in the studied groups

The studied gene		Control group n=80 (%)	Experimental group 1 (with phenotypic signs of UDCT) n=44 (%)	Experimental group 2 (with anastomotic leak) n=17 (%)
MMP2 ($C^{-1306} \rightarrow T$)	CC	38 (47,5%)	26 (59,1%)	11 (64,7%)
	CT	34 (42,5%)	16 (36,4%)	5 (29,4%)
	TT	8 (10%)	2 (4,5%)	1 (5,9%)
Hardy-Weinberg test (χ^2, p)		χ^2=0,01, p>0,05	χ^2=0,05, p>0,05	χ^2=0,17, p>0,05
TIMP2 ($G^{303} \rightarrow A$)	GG	50 (50%)	24 (54,5%)	14 (82,4%)
	GA	32 (40%)	15 (34,1%)	3 (17,6%)
	AA	8 (10%)	5 (11,4%)	0 (%)
Hardy-Weinberg test (χ^2, p)		χ^2=0,18, p>0,05	χ^2=1,15, p<0,05	χ^2=0,15, p<0,05

Table 2. The odds ratio for a recessive model of inheritance of patients with phenotypic signs of UDCT. Odds ratio with 95% confidence interval

Genotype	Control group n=80 (%)	Experimental group 1 (with phenotypical signs of UDCT)n=44 (%)	Odds ratio	p-value	AIC
CC+CT	72 (90%)	42 (95.5%)	1.00		
TT	8 (10%)	2 (4.5%)	0.43 (0.06 - 1.81)	0.3	16.12

Table 3. The odds ratio for the recessive model of inheritance in patients with failure of anastomotic sutures. Odds ratio with 95% confidence interval

Genotype	Control group n=80 (%)	Experimental group 2 (with anastomotic leak) n=17 (%)	Odds ratio	p-value	AIC
CC+CT	72 (90%)	16 (94.1%)	1.00		
TT	8 (10%)	1 (5.9%)	0.56 (0.03 - 3.39)	0.6	14.62

Analysis of the multiplicative model of inheritance of the MMP-2 gene ($C^{-1306} \rightarrow T$), comparing the control group (n=80) and experimental group 2 with anastomotic leak (n=17) showed compliance with the distribution of genotypes to Hardy-Weinberg's law (p>0,05), which was tested in the control group using the test $\chi 2$ with 1 degree of freedom, without Yates correction. Using the test $\chi 2$ with 2 degrees of freedom, we did not find statistically significant differences in the distribution of genotypes in the group of sick people and the group of practically healthy people (p>0.05). After analyzing all models of inheritance, we chose the best model with the lowest AIC (Table 3).

It is noteworthy that in experimental groups 1 and 2 there were half as many carriers of the homozygous TT genotype as compared with the control: 4.4% and 5.9% versus 10% (p<0.05), respectively. However, carriers of the SS genotype dominant in all groups were greater in the group with suture failure (research 2): 64.7% versus 47.5% (p<0.05) in the control (Fig. 1).

In the analysis of TIMP-2 inheritance models ($G^{303} \rightarrow A$), in the control group (n = 80) and experimental group 1 with phenotypic signs of connective tissue pathology (n = 44), we could not find statistically significant differences in the distribution of genotypes in the group of patients and the group of almost healthy people (p>0.05). The conformity of the genotype distribution to Hardy-Weinberg's law in the control group was checked using the $\chi 2$ test with 1 degree of freedom, without the use of Yates correction. It was found that the distribution of genotypes in the control group corresponds to Hardy-Weinberg's law (p>0.05).

We were able to find statistically significant differences in the distribution of genotypes (p<0.05) in the analysis of TIMP-2 inheritance models ($G^{303} \rightarrow A$), in the control group (n=80) and experimental group 2 with anastomotic leak (n=17). The conformity of the genotype distribution to Hardy-Weinberg's law in the control group was checked using the $\chi 2$ test with 1 degree of freedom, without the use of Yates correction. After analyzing all models of inheritance, we chose the best model with the lowest AIC (Table 4).

In the examined population in the control group and experimental group 1, the distribution of carriers of GG, GA, and AA genotypes was significantly similar. However, in the group of patients with anastomotic leak (experimental group 2), the distribution of genotype carriers was significantly different. Thus, the dominant GG variant almost twice significantly exceeded the indicators of control and experimental group 1 (82.4% vs. 50% and 54.4%, respectively, p<0.05). Heterozygous GA genotype in the second experimental group was more than twice as rare as in the control (17.6% vs. 40%). Carriers of homozygous AA genotype in the group with anastomotic leak were not detected, while a similar variant in control and experimental group 1 was found in 10% and 11.4% of cases (Fig. 2).

In examined patients with anastomotic leak of the hollow digestive organs, signs of UDCT were found in 13 (76.47%) patients. The following phenotypic pathologies of UDCT were most commonly encountered: visceral pathology (76.47%), vascular pathology (70.58%), arrhythmias (52.9%).

The study of phenotypic signs of UDCT in the group of patients with anastomotic leak showed that 3 patients (17.6%) had a mild UDCT, 6 patients (35.3%) had moderate, and 4 patients (23.6%) had a severe degree of UDCT. In 4 patients (23.5%), signs of the pathology of the connective tissue were not detected.

The level of serum hydroxyproline in the group of patients without phenotypic signs of connective tissue dysplasia was 36.9±1.6 μmol/L, which is almost twice as high as in the control group (21.2±0.8 μmol/L). When studying the dynamics of changes in serum hydroxyproline levels, it was found that an increase in the collagenolytic activity of glycosaminoglycans and free hydroxyproline levels had a direct correlation with the severity of UDCT. With a mild degree of UDCT, the level of serum hydroxyproline was (46.9±2.8) μmol/L, moderate (75.2±3.2) μmol/L and severe (122.1±3.6) μmol/l, which is almost 6 times higher than in the control group and 3 times higher than in patients with anastomotic leak without clinical signs of connective tissue dysplasia.

When studying the dynamics of changes in urinary glycosaminoglycans levels, a direct correlation with the severity of UDCT was also revealed. With a mild degree of UDCT, the level of glycosaminoglycans was 80.94±2.8 μmol/L, which is highly reliable, twice as many as in the control group (44.68±1.8). With an average degree of 105.12±3.5 μmol/L and a severe degree of 127.54±3.4 μmol/L, which was almost 3 times higher than the control group and 2 times higher than patients with anastomotic leak without clinical signs of connective tissue dysplasia.

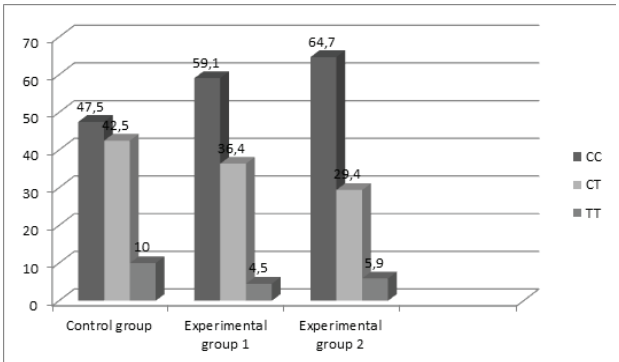

Fig. 1. Frequency distribution of allelic polymorphism (%) of the promoter ($C^{-1306} \rightarrow T$) MMP2 gene

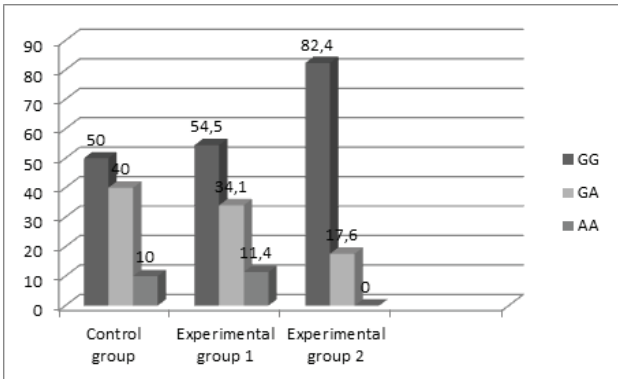

Fig. 2. Frequency distribution of allelic polymorphism (%) of the promoter ($G^{303} \rightarrow A$) of the TIMP2 gene

Table 4. The odds ratio for recessive inheritance model in patients with anastomotic leak. Odds ratio with 95% confidence interval

Genotype	Control group n=80 (%)	Experimental group 2 (with anastomotic leak) n=17 (%)	Odds ratio	p-value	AIC
GG+GA	72 (90%)	17 (100%)	1.00		
AA	8 (10%)	0 (0%)	0 (NA-1.479e+266)	1	15.62

Our data on the study of polymorphic variants of the MMP2 ($C^{-1306} \rightarrow T$) and TIMP2 ($G^{303} \rightarrow A$) genes in the Ukrainian population (n = 80) generally correspond to populations of Europe and the USA [23,24].

The closest genotypic variations in the studied genes were populations of Austria [25] and the Netherlands [26]. Moreover, we found significant differences when compared with the African and Asian populations [27,28]. Interestingly, in these populations, the frequency of the main C allele of the MMP-2 gene (rs243865) was 93.7% (Africa) and 90% (Asia), which significantly exceeds the indices of our control group (76%) and the European population (75,5%). Whereas, the minor T allele was found in 24% of the control group, and 10% (Asia) and 6.7% (Africa), respectively [23].

As a result of genetic and statistical analysis of the polymorphism of the MMP-2 ($C^{-1306} \rightarrow T$) and TIMP-2 ($G^{303} \rightarrow A$) genes, variants of genotypes associated with the risk of development of anastomotic leak of the hollow digestive organs were determined.

Thus, in the experimental group with anastomotic leak, carriers of the homozygous SS genotype of the MMP2 gene were found to be 1.36 times more often than in the control group. At the same time, the minor TT homozygotes in the group of patients with anastomotic leak were almost half that in the control (5.9% versus 10% ($p < 0.05$)).

In the analysis of carriers of TIMP-2 genotypes, we obtained statically reliable data: in the group of patients with anastomotic leak, GG variant was 82.4%, which is 1.6 times higher than in the control group (82.4% vs. 54.4%, $p<0.05$). Carriers of minor homozygotes of AA genotype in the group of patients with anastomotic leak were not detected, while a similar genotype in the control group was found in 10%.

Given the role of matrix metalloproteinases and their inhibitors in the processes of synthesis and proteolysis, connective tissue remodeling, connective tissue protein metabolism, the ability to affect vascular permeability and angiogenesis, [8] the relevance of their study in the context of the pathogenesis of anastomotic leak of the hollow digestive organs is undoubted.

There are several publications in the literature on the detection of changes in the ratio of type I/III collagen, increased expression of MMP-1 and MMP-2 in the mucosa and MMP-2 and MMP-9 in the submucosal layer of the colon in patients with the leakage of colorectal anastomosis [17-19].

The correlation between the level of biochemical markers of collagen biodegradation and the severity of UDST revealed, which is diagnosed on the basis of phenotypic, visceral manifestations, and instrumental examinations. This could serve as an informative diagnostic criterion of UDST and could be used to predict the development and course of complications in patients with anastomotic leak in the hollow digestive organs. Such changes are apparently due to increased proteolytic activity in patients with anastomotic leak. This confirms the data of some authors that the anastomotic leak and development of peritonitis leads to a pronounced and persistent mismatch in the proteinase system - inhibitors of blood proteinases. It is the hyperactivation of proteolytic systems of the body against the background of reduction of inhibitory potential that is regarded as one of the key pathogenetic links of endogenous intoxication.

Understanding the pathogenetic processes underlying the formation of the anastomosis and possible «weaknesses» is no less important than the surgical technique.

In our view, the focus of future research on the pathogenetic factors of abdominal postoperative complications should be shifted to a more cellular and molecular level. Thus, a better understanding of the mechanisms of the formation of intestinal anastomosis will contribute to the development of new diagnostic, prognostic, and therapeutic techniques.

The differences we have identified in allelic variants of the studied genes in the groups with anastomotic leak are the basis for further study and research for molecular genetic markers that encode the main links in the pathogenesis of anastomotic leak and other postoperative complications.

Conclusions.

1. Anastomotic leak in hollow digestive organs is 1.36 times more common in carriers of homozygous CC genotype of the MMP-2 gene, and twice less common in minor homozygotes of TT (5.9% vs. 10%, $p>0,05$).

2. In the group of patients with anastomotic leak in hollow digestive organs, it is statistically significant, the GG variant of the TIMP-2 gene was detected 1.6 times more often. Carriers of minor homozygotes of AA genotype in the group with anastomotic leak were not detected, while a similar genotype in the control group was found in 10% ($p<0,05$).

3. Molecular genetic research can be a new promising area for the development of modern personalized diagnostic criteria and models for predicting the development and course of postoperative abdominal complications, including the anastomotic leak of the hollow digestive organs.

4. The presence of connective tissue dysplasia in patients with anastomotic leak in the hollow digestive organs is an aggravating comorbid factor, which must be considered when choosing adequate surgical tactics and complex pathogenetically substantiated treatment.

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REFERENCES

1. Boyko VV, Leonov AV, Taraban IA et al. Nespromozhnist kyshkovykh anastomoziv. Kharkivska khirurhichna shkola. 2013;6(63):5-8. [In Ukrainian].
2. Shalkov YuL, Leonov VV. Kyshechnye shvy y anastomozy v khyrurhycheskoi praktyke. Kharkov: Kollehyum; 2008. — 192 p. [In Russian].
3. Pitel S, Lefèvre JH, Tiret E. Redo coloanal anastomosis: a retrospective study of 66 patients. Ann Surg. 2012; 256 (5):806-811.
4. Sharonne de Z, Usama AA, Rogier AR. Update of complications and functional outcome of the ileo-pouch anal anastomosis: overview of evidence and meta-analysis of 96 observational studies. Int. J. Colorectal Dis. 2012;27:843-853.
5. Melnyk VM, Poida OI. Khirurhichna taktyka pry nespromozhnosti shviv mizhkyshkovykh anastomoziv. Klinichna khirurhiia. 2016; №6:8-12. [In Ukrainian].
6. Alekseeva NT, Hlukhov AA, Ostroushko AP. Rol kletok fybroblastycheskoho dyfferona v protsesse zazhyvlenyia ran. Vestnyk eksperymentalnoi y klynycheskoi khyrurhyy. 2012; 5(3): 601–608. [In Russian].
7. Marjanovic, G., Hopt, U. Physiologie der Anastomosenheilung. Chirurg 82, 41–47 (2011). https://doi.org/10.1007/s00104-010-1898-2.
8. Growth factors and gastrointestinal anastomotic heal-

ing. J Surg Res. 2014 Mar;187(1):202-10. doi: 10.1016/j.jss.2013.10.013. Epub 2013 Oct 12.
9. Visse R, Nagase H. Matrix metalloproteinases and tissue inhibitors of metalloproteinases: structure, function, and biochemistry. Circulation Res. 2003;2: 827-39.
10. Fassina G, Ferrari N, Brigati C, et al. Tissue inhibitors of metalloproteases: Regulation and biological activities. Clin Experim Metastas 2000; 18: 111–20.
11. Chen GL, Wang SC, Shen TC et al. The association of matrix metalloproteinas-2 promoter polymorphisms with lung cancer susceptibility in Taiwan. Chin J Physiol 2019;62:210-6
12. Banday MZ, Sameer AS, Mir AH, et al. Matrix metalloproteinase (MMP) -2, -7 and -9 promoter polymorphisms in colorectal cancer in ethnic Kashmiri population - A case-control study and a mini review. Haq E.Gene. 2016 Sep 1; 589(1):81-89. Epub 2016 May 21.
13. Zhang K, Chen X, Zhou J et al. Association between MMP2-1306 C/T polymorphism and prostate cancer susceptibility: a meta-analysis based on 3906 subjects. Oncotarget. 2017 Jul 4; 8(27):45020-45029.);
14. Beton O, Arslan S, Acar B et al. Association between MMP-3 and MMP-9 polymorphisms and coronary artery disease. Biomed Rep. 2016;5:709-14.
15. Yi Z, Yi H, Xue C, Zhi Z. Association between matrix metalloproteinase-8 -799C/T polymorphism and instability of carotid plaque. Ather Risk Comm. 2012;29(1):60-63.),
16. Liutkeviciene R, Lesauskaite V, Sinkunaite-Marsalkiene G et al. The Role of Matrix Metalloproteinases Polymorphisms in Age-Related Macular Degeneration. Ophthalmic Genet. 2015. June;36(2):149–55.).
17. Stumpf M, Junge K, Wendlandt M et al. Risk factors for anastomotic leakage after colorectal surgery. Zentralbl Chir. 2009 Jun; 134(3):242-8. Epub 2009 Jun 17.
18. Stumpf M, Cao W, Klinge U et al. Collagen distribution and expression of matrix metalloproteinases 1 and 13 in patients with anastomotic leakage after large-bowel surgery. Arch Surg. 2002 Jan; 386(7):502-6. Epub 2001 Nov 8.
19. Agren MS, Andersen TL, Mirastschijski U et al. Action of matrix metalloproteinases at restricted sites in colon anastomosis repair: an immunohistochemical and biochemical study. Surgery. 2006 Jul; 140(1):72-82.
20. Hirahara I, Inoue M, Okuda K et al. The potential of matrix metalloproteinase-2 as a marker of peritoneal injury, increased solute transport, or progression to encapsulating peritoneal sclerosis during peritoneal dialysis--a multicentre study in Japan. Nephrol Dial Transplant. 2007 Feb; 22(2):560-7. Epub 2006 Oct 11.
21. J. Hästbacka, M. Hynninen, E. Kolho et al. Collagenase 2/ matrix metalloproteinase 8 in critically ill patients with secondary peritonitis. Shock. 2007 Feb;27(2):145-50.
22. Usenko OYu, Voitiv Ya.Yu. Chastota ta kryterii diahnostyky nedyferentsiiovanoi dysplazii spoluchnoi tkanyny u khvorykh khirurhichnoho statsionaru. Klinichna khirurhiia. 2017; 10: 5-7. [In Ukrainian]. DOI: https://doi.org/10.26779/2522-1396.2017.10.05
23. Population Diversity (Alleles in RefSNP orientation) / dbSNP Short Genetic Variation // NCBI. – 2017. – URL: https://www.ncbi.nlm.nih.gov/snp/rs243865;
24. Population Diversity (Alleles in RefSNP orientation) / dbSNP Short Genetic Variation // NCBI. – 2017. – URL: https://www.ncbi.nlm.nih.gov/snp/rs9900972
25. Mossbock G. Weger M. Faschinger C. Zimmermann C. Schmut O. Renner W. El-Shabrawi Y. Role of functional single nucleotide polymorphisms of MMP1, MMP2, and MMP9 in open angle glaucomas. Mol Vis. 2010;16).
26. van Diemen CC. Postma DS. Siedlinski M. Blokstra A. Smit HA. Boezen HM. Genetic variation in TIMP1 but not MMPs predict excess FEV1 decline in two general population-based cohorts.Respir Res. 2011;12:57.).
27. Xu E. Lai M. Lv B. Xing X. Huang Q. Xia X. A single nucleotide polymorphism in the matrix metalloproteinase-2 promoter is associated with colorectal cancer. Biochem Biophys Res Commun.2004;324:999–1003;
28. Li Y, Sun DL, Duan YN et al. Association of functional polymorphisms in MMPs genes with gastric cardia adenocarcinoma and esophageal squamous cell carcinoma in high incidence region of North China. Mol Biol Rep. 2010 Jan; 37(1):197-205.).

SUMMARY

ANALYSIS OF POLYMORPHISM OF MATRIX METALLOPROTEINASE-2 ($C^{-1306} \rightarrow T$) AND TISSUE INHIBITORS OF METALLOPROTEINASE-2 ($G^{303} \rightarrow A$) GENES IN PATIENTS WITH ANASTOMOTIC LEAK IN HOLLOW DIGESTIVE ORGANS

[1]Voitiv Y., [2]Usenko O., [3]Dosenko V., [1]Dyadyk O., [2]Dzhemiliev A.

[1]Shupyk National Academy of Postgraduate Educationof the Ministry of Health of Ukraine, Kyiv; [2]Shalimov National Institute of Surgery and Transplantology, National Academy of Medical Sciences of Ukraine, Kyiv; [3]Bogomoletz Institute of Physiology, National Academy of Sciences of Ukraine, Kyiv, Ukraine

The aim. To analyze the frequency of polymorphic variants of MMP-2 ($C^{-1306} \rightarrow T$) and TIMP-2 ($G^{303} \rightarrow A$) genes in patients with anastomotic leak in hollow digestive organs.

The object of the study comprises 61 patients with anastomotic leak and connective tissue pathology, all treated at the Shalimov National Institute of Surgery and Transplantology during 2016-2019. Laboratory, genetic, histological studies and statistical analysis were performed.

As a result of genetic and statistical analysis of the MMP-2 ($C^{-1306} \rightarrow T$) and TIMP-2 ($G^{303} \rightarrow A$) gene polymorphisms, genotype variants have been identified that are associated with the risk of anastomotic leak in hollow digestive organs. Significant differences in the distribution of genotypes in the studied groups were revealed. Analysis of the multiplicative model of inheritance of MMP-2 and TIMP-2 genes showed compliance of genotype distribution with Hardy-Weinberg's law. All models of inheritance were analyzed and the best model with the lowest Akaike Information Criterion, which turned out to be a recessive model, has been determined.

Anastomotic leak in hollow digestive organs is 1.36 times more common in carriers of homozygous CC genotype of the MMP-2 gene and twice less common in minor homozygotes of TT (5.9% vs. 10%, $p>0.05$). It is statistically significant that in the group of patients with anastomotic leak in hollow digestive organs the GG variant of the TIMP-2 gene was detected 1.6 times more often. Carriers of minor homozygotes of AA genotype in the group with suture failure were not detected, while a similar genotype in the control group was found in 10% ($p<0.05$).

Keywords: Anastomotic leak, MMP-2, TIMR-2, gene polymorphism.

РЕЗЮМЕ

АНАЛИЗ ПОЛИМОРФИЗМА ГЕНОВ МАТРИКСНОЙ МЕТАЛЛОПРОТЕИНАЗЫ - 2 (C^{-1306}→T) И ТКАНЕВОГО ИНГИБИТОРА МАТРИКСНОЙ МЕТАЛЛОПРОТЕИНАЗЫ - 2 (G^{303}→A) У БОЛЬНЫХ С НЕСОСТОЯТЕЛЬНОСТЬЮ ШВОВ АНАСТОМОЗОВ ПОЛЫХ ОРГАНОВ ПИЩЕВАРЕНИЯ

[1]Войтив Я.Ю., [1]Усенко О.Ю., [2]Досенко В.Э., [1]Дядык О.О., Джемилев А.И.

[1]Национальная медицинская академия последипломного образования им. П.Л. Щупика;
[2]ГУ «Национальный институт хирургии и трансплантологии им. А.А. Шалимова» НАМН Украины;
[3]Институт физиологии им. А.А. Богомольца НАН Украины, Киев, Украина

Цель исследования - анализ частоты полиморфных вариантов генов матриксной металлопротеиназы – 2 (C^{-1306}→T) и тканевого ингибитора матриксной металлопротеиназы - 2 (G^{303}→A) у больных с несостоятельностью швов анастомозов полых органов пищеварения.

Обследован 61 пациент с несостоятельностью швов анастомозов (n=17) и патологией соединительной ткани (n=44), которые лечились в Национальном институте хирургии и трансплантологии им. А.А. Шалимова. Проведены лабораторные, генетические, гистологические и статистические исследования.

В результате генетического и статистического анализа полиморфизма генов матриксной металлопротеиназы – 2 (C^{-1306}→T) и тканевого ингибитора матриксной металлопротеиназы – 2 (G^{303}→A) определены варианты генотипов, ассоциированных с риском развития несостоятельности швов анастомозов полых органов пищеварения. Выявлены достоверные различия распределения генотипов в изучаемых группах. Анализ мультипликативной модели наследования генов матриксной металлопротеиназы – 2 (C^{-1306}→T) и тканевого ингибитора матриксной металлопротеиназы – 2 (G^{303}→A) показал соответствие распределения генотипов с законом Харди-Вайнберга. Проанализированы все наследственные модели, лучшей среди них с наиболее низким информационным критерием Акаики оказалась рецессивная модель.

Несостоятельность швов анастомозов полых органов пищеварения в 1,36 раза чаще встречается у носителей гомозиготного СС генотипа гена матриксной металлопротеиназы – 2 (C^{-1306}→T) и вдвое реже - в минорных гомозиготах ТТ (5,9% против 10%, p<0,05). В группе пациентов с несостоятельностью швов анастомозов полых органов пищеварения, статистически достоверно, в 1,6 раза чаще выявлены носители гомозиготного GG варианта гена тканевого ингибитора матриксной металлопротеиназы – 2 (G^{303}→A). Носителей минорных гомозигот АА генотипа в группе с несостоятельностью швов не обнаружено, аналогичный генотип в контрольной группе встречался в 10% (p<0,05).

რეზიუმე

მატრიქსული მეტალოპროტეინაზა-2-ის და მატრიქსული მეტალოპროტეინაზა-2-ის ქსოვილური ინჰიბიტორის გენების პოლიმორფიზმი პაციენტებში საჭმლის მომნელებელი ღრუ ორგანოების ანასტომოზების ნაკერების უკმარისობით

[1]ი. ვოიტივი, [1]ო. უსენკო, [2]ვ. დოსენკო, [1]ო. დიადიკი, [2]ა. ჯემილევი

[1]პ. შუპიკის სახ. დიპლომისშემდგომი განათლების ეროვნული სამედიცინო აკადემია;
[2]ა. შალიმოვის სახ.ქირურგიისა და ტრანსპლანტოლოგიის ეროვნული ინ-სტიტუტი;
[3]ა. ბოგომოლეცის სახ. ფიზიოლოგიის ინსტიტუტი, კიევი, უკრაინა

კვლევის მიზანს წარმოადგენდა მატრიქსული მეტალოპროტეინაზა-2-ის (C^{-1306}→T) და მატრიქსული მეტალოპროტეინაზა-2-ის ქსოვილური ინჰიბიტორის (G^{303}→A) გენების პოლიმორფული ვარიანტების სიხშირის ანალიზი პაციენტებში საჭმლის მომნელებელი ღრუ ორგანოების ანასტომოზების ნაკერების უკმარისობით. გამოკვლეულია 61 პაციენტი ანასტომოზების ნაკერების უკმარისობით (n=17) და შემაერთებელი ქსოვილის პათოლოგიით (n=44), რომლებიც მკურნალობდნენ ა. შალიმოვის სახ. ქირურგიისა და ტრანსპლანტოლოგიის ეროვნულ ინსტიტუტში. ჩატარებულია ლაბორატორიული, გენეტიკური, ჰისტოლოგიური და სტატისტიკური კვლევები. მატრიქსული მეტალოპროტეინაზა-2-ის (C^{-1306}→T) და მატრიქსული მეტალოპროტეინაზა-2-ის ქსოვილური ინჰიბიტორის (G^{303}→A) გენების პოლიმორფიზმის გენეტიკური და სტატისტიკური ანალიზის საფუძველზე განსაზღვრულია გენოტიპების ვარიანტები,დაკავშირებული საჭმლის მომნელებელი ღრუ ორგანოების ანასტომოზების ნაკერების უკმარისობის განვითარების რისკთან. გამოვლენილია გენოტიპების განაწილების სარწმუნო განსხვავება შესწავლილ ჯგუფებს შორის. მატრიქსული მეტალოპროტეინაზა-2-ის (C^{-1306}→T) და მატრიქსული მეტა-ლოპროტეინაზა-2-ის ქსოვილური ინჰიბიტორის (G^{303}→A) გენების დამემკვიდრების მულტიპლიკაციური მოდელის ანალიზმა აჩვენა გენოტიპების განაწილების შესაბამისობა ჰარდი-ვაინბერგის კანონთან. გაანალიზებულია დამემკვიდრების ყველა მოდელი; მათ შორის ყველაზე კარგი, აკაიკის ყველაზე დაბალი ინფორმაციული კრიტერიუმით, აღმოჩნდა რეცესიული მოდელი. საჭმლის მომნელებელი ორგანოების ანასტომოზების ნაკერების უკმარისობა 1,36-ჯერ უფრო ხშირია მატრიქსული მეტალოპროტეინაზა-2-ის (C^{-1306}→T) გენის ჰომოზიგოტური СС გენოტიპის მტარებლებში და ორჯერ უფრო იშვიათი - ТТ მინორულ ჰომოზიგოტებში (5,9% *vs* 10%, p<0,05). საჭმლის მომნელებელი ღრუ ორგანოების ანასტომოზების ნაკერების უკმარისობის მქონე პაციენტების ჯგუფში სტატისტიკურად სარწმუნოდ 1,6-ჯერ უფრო ხშირია მატრიქსული მეტალოპროტეინაზა-2-ის (G^{303}→A) გენის ჰომოზიგოტური GG ვარიანტის მტარებლები. АА გენოტიპის მინორული ჰომოზიგოტების მტარებლები ნაკერების უკმარისობის მქონეთა ჯგუფში არ გამოვლენილა; საკონტროლო ჯგუფში ანალოგიური გენოტიპის სიხშირემ შეადგინა 10% (p<0,05).