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Clinical and vegetative disorders, adaptive capacity and stress resistance in patients with precancerous conditions of the stomach in comorbidity with thyroid pathology

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Abstract. Background. An important aspect of the course of precancerous conditions of the stomach is comorbidity with thyroid pathology. To date, there is no consensus among researchers regarding the involvement of the autonomic nervous system in ensuring the reactivity of the body and the formation of adaptive processes in patients with atrophic gastritis combined with thyroiditis. The purpose was to determine the features of clinical manifestations, autonomic status and heart rate variability in patients with precancerous conditions of the stomach in comorbid thyroid pathology. **Materials and methods.** The study included 72 patients with chronic atrophic gastritis, who were divided into 3 groups depending on the changes in the structure of the thyroid gland: group I consisted of 35 people with nodular changes, II — 22 with diffuse changes, III — 15 people without any changes. To study the clinical picture in the examined patients, a survey was conducted using the Gastrointestinal Symptom Rating Scale. To identify signs of autonomic disorders, we used the questionnaire of O.M. Vein. Adaptive capacity was assessed using Precise system on a CONTEC 8000GW cardiograph with software that analyzes heart rate variability. **Results.** In patients with comorbid pathology, symptoms of abdominal pain syndrome and dyspeptic syndrome were often revealed regardless of structural changes in the thyroid gland; the frequency of diarrheal syndrome in group I was 1.9 times lower than in group II ($p = 0.02$) and 1.8 times compared with group III ($p > 0.05$). A high frequency of autonomic dysfunction (83.3 %) was detected in patients with precancerous conditions of the stomach. At the same time, individuals with nodular changes in the thyroid gland quite often complained of decreased performance, rapid fatigue (68.6 %) and sleep disturbances (65.7 %). Patients with diffuse changes in the thyroid gland had numbness of the fingers and toes (68.2 %), a tendency to facial redness and increased sweating (63.6 %). Correlations were determined between the score on Vein's questionnaire and the severity of syndromes such as abdominal pain ($r = 0.53$; $p = 0.030$), diarrheal syndrome ($r = 0.58$; $p = 0.012$), dyspeptic syndrome ($r = 0.44$, $p = 0.029$). Analysis of stress resistance showed that 33.3 % of patients with nodular changes in the thyroid gland and 28.6 % of those with diffuse changes had anxiety syndrome, while people without thyroid pathology had no anxiety. **Conclusions.** According to Precise system data, half of patients with precancerous conditions of the stomach in thyroid comorbidity have an increased cardiovascular risk against the background of an increase in parasympathetic regulation of the autonomic nervous system, and one-third of patients have a breakdown/disorder of adaptation, anxiety syndrome and depletion of the sympathetic and parasympathetic components of the autonomic nervous system. The revealed correlations indicate a significant contribution of autonomic disorders to the formation of clinical symptoms in patients with comorbid pathology of the stomach and thyroid gland.

Keywords: autonomic dysfunction; adaptive capabilities; stress resistance; precancerous conditions of the stomach; thyroid pathology

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Introduction

An important aspect of chronic gastritis and precancerous conditions is comorbidity, that is the course of several diseases, either united by single pathogenesis, or initially independent, but able to exert bilateral influence on each other [1–3].

The thyroid gland and stomach are derived from the same part of the early embryo — the primitive intestine, which combines their properties. Thyroid cells and the stomach have common functions, namely the transport of iodine, which in turn helps produce glandular hormones and promotes cell proliferation in the stomach [4, 5].

In the presence of comorbid pathology, precancerous conditions of the stomach (atrophic gastritis, intestinal metaplasia of the gastric mucosa) in most patients are asymptomatic, which causes difficulties in timely diagnosis. The important point is also no specific pathognomonic clinical manifestations of severe gastritis with dysplastic changes [8, 9].

One of the factors that can play a significant role in the course of comorbid diseases through neuro-humoral regulation is the autonomic nervous system (ANS). The term “autonomic nervous system” was coined in 1801 by the French physician M. Bichat. He defined the ANS as a department of the central nervous system that regulates body functions and includes three components: sympathetic, parasympathetic and metasympathetic. ANS maintains the stability of the internal environment of the body and provides various forms of mental and physical activity [10, 11].

In his study, M.D. Petrash with co-authors came to the conclusion that in a situation of daily stress, the sympathetic nervous system creates conditions for mobilization of energy resources, activates functional responses to stimuli, and the parasympathetic system performs a corrective function, maintains homeostasis, provides reserves for emergency regulation [12].

It is known that morpho-functional formations of the autonomic nervous system are located throughout the body, providing its adaptive-trophic organization. In this case, for the formation of long-term adaptation, in addition to increasing self-regulation mechanisms, it is extremely important to increase the reactivity of functioning systems. Reduced adaptation is a feature of various dysregulations in pathological conditions, in particular precancerous lesions. The role of the regulatory impact of the ANS with gastrointestinal diseases has been confirmed in many studies of atrophic gastritis. Thus, chronic gastritis with moderate focal atrophy of the mucous membrane is accompanied by autonomic eutonia, and chronic gastritis with widespread atrophy of the mucous membrane is characterized by sympatheticotonia [13].

Also, the researchers still have no consensus on the participation of the autonomic nervous system in ensuring the reactivity of the body and the formation of adaptive processes in patients with thyroid pathology. According to S.M. Voronich with co-authors, a correlation was found between the content of thyroid hormones in the serum and heart rate variability, which confirms the essential role of thyroid hormones in ensuring the functional capacity of the autonomic nervous system [14].

Therefore, studying pathogenesis of precancerous conditions of the stomach in patients with comorbid pathology of the thyroid gland from the standpoint of the functional state of the ANS is relevant and promising.

The purpose of the study was to determine the features of clinical manifestations, autonomic status and heart rate variability in patients with precancerous conditions of the stomach in comorbid pathology of the thyroid gland.

Material and methods

The study included 72 patients with chronic atrophic gastritis, who were divided into 3 groups depending on changes in the structure of the thyroid gland: group I consisted of 35 people with nodular changes, II — 22 with diffuse changes, III — 15 people without any changes. The examined patients included mostly women: in group I — 27 (77.1 %), II — 17 (77.3 %), III — 12 (80.0 %). The patients in group I were significantly older than those in groups II and III. The average age was as follows: group I — (63.2 ± 1.4) years, group II — (56.0 ± 2.5) years ($p = 0.026$ compared to group I), group III — (52.1 ± 2.9) years ($p = 0.008$ compared to group I). An increase in the average age of patients of group I is due to growing age group of persons over 61 years. In group I, there were 68.6 % ($n = 24$) of such individuals, while in group II — 1.9 times less, 36.4 % ($n = 8$) ($\chi^2 = 5.69$, $p < 0.05$), and in group III — 2.6 times less, 26.7 % ($n = 4$) ($F = 0.012$, $p < 0.05$).

To study the clinical picture in the examined patients, a survey was conducted using the Gastrointestinal Symptom Rating Scale (GSRS), which included 15 questions about symptoms the severity of which was determined by the 7-point Likert scale. When analyzing the results, the responses were evaluated by the manifestations of abdominal pain syndrome, reflux syndrome, dyspeptic syndrome, diarrheal syndrome, constipation syndrome and by assessing their severity.

To identify signs of autonomic disorders, we have used a questionnaire of O.M. Vein, which allows investigating autonomic stability (lability of the thermoregulatory system, vestibular system, signs of anxiety, pain symptoms) and assessing the severity of autonomic dysfunction with a score of symptoms. In healthy individuals, the sum of points should not exceed 15.

Adaptive capacity was assessed using Precise system (Cloud Automated Interpretation Technology) on a CONTEC 8000GW cardiograph with Bluetooth connection and software, with heart rate variability analysis by means of an automated ECG interpretation program ($n = 25$). Interpretation of indicators of Precise system is given in Table 1.

Statistical analysis was performed by means of Excel Microsoft Office 2010 using the methods of variation statistics. Data are presented as mean (M) and error in calculating the average (m). For comparison of quantitative performance criterion, Mann-Whitney and Kruskal-Wallis tests were used. To compare qualitative data, χ^2 or F tests were applied. The difference was considered statistically significant at the achieved level of probability not lower than 95.0 %. Correlation analysis was performed with the calculation of Spearman's rank correlation coefficient (r) and its significance (p).

Results and discussion

According to the GSRS, patients with precancerous changes in gastric mucosa showed significant symptoms of both abdominal pain and dyspeptic syndrome, in most cases in combination with reflux. Such data may complicate the diagnosis of precancerous conditions at the stage of collecting patient complaints. In addition, there was no significant difference in the frequency of main syndromes in patients with comorbid pathology (Table 2), except for diarrheal syndrome, the frequency of which in group I was 1.9 times lower than in group II ($p = 0.02$), and 1.8 times — compared with group III ($p > 0.05$).

In addition, according to Fig. 1, patients of group III have a higher intensity of dyspeptic syndrome — (15.00 ± 1.92) points compared with group I — (11.10 ± 1.07) points

($p < 0.05$). The significance of the difference between the three groups according to the Kruskal-Wallis test was 0.022. Diarrheal syndrome was more severe in patients of group II — (6.50 ± 0.44) points compared with group I — (4.40 ± 0.31) ($p < 0.05$). The significance of the difference between 3 groups according to the Kruskal-Wallis criteria for these symptoms was 0.025.

The evaluation of Precise system data revealed a decrease in LF/HF ratio in groups I and II to (0.52 ± 0.08) ms and (0.56 ± 0.76) ms, respectively, indicating the prevalence of parasympathetic regulation in patients with comorbid pathology. Most individuals with precancerous gastric conditions without combined thyroid pathology had eutonia, which indicates the balance of the sympathetic and parasympathetic divisions of the ANS (Table 3).

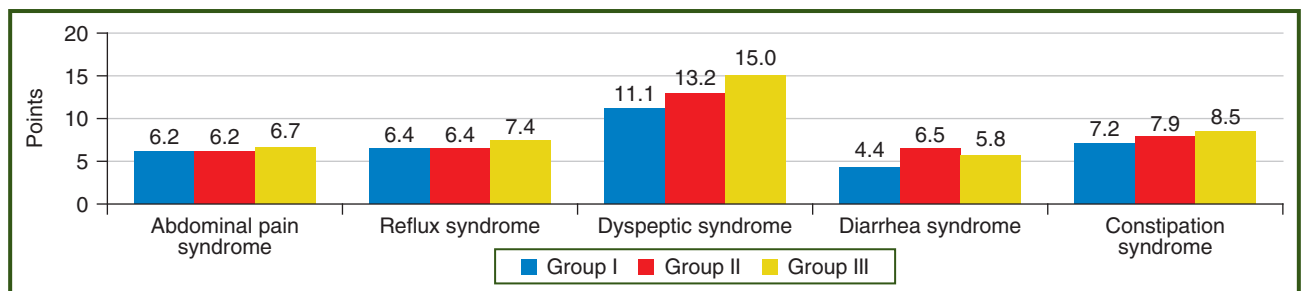


Figure 1 — Severity of main syndromes in groups, average score

Table 1 — The main indicators of heart rate variability

Indicator	Value	Interpretation
SDNN — standard deviation of the values of normal NN intervals	up to 20 ms	significant cardiovascular risk
	20–50 ms	increased cardiovascular risk
	more than 50 ms	norm
RMSSD — the square root of the mean square of the difference of the values of successive pairs of NN intervals	up to 20 ms	failure/violation of adaptation
	20–100 ms	normal adaptation
	more than 100 ms	good physical training
LF/HF — the ratio of low-frequency oscillations of autonomic heart rate to high-frequency oscillations	up to 0.9	vagotonia
	0.9–1.6	normotonia
	more than 1.6	sympathicotonia
Total power — total power of the spectrum	up to 1500	exhaustion
	1,500–10,000	resource state
	more than 10,000	hormonal imbalance
Stress index — an indicator of stress resistance	up to 100 ms	norm
	100–400 ms	anxiety
	more than 400 ms	pain syndrome

Table 2 — Characteristics of symptoms in groups, n (%)

Symptoms	Group I (n = 35)	Group II (n = 22)	Group III (n = 15)
Abdominal pain syndrome	33 (94.3)	22 (100.0)	15 (100.0)
Reflux syndrome	27 (77.1)	18 (75.0)	10 (66.7)
Dyspeptic syndrome	34 (97.1)	22 (100.0)	15 (100.0)
Diarrheal syndrome	13 (37.1)*	16 (72.7)	10 (66.7)
Constipation syndrome	25 (71.4)	17 (77.3)	12 (80.0)

Note. * — $p < 0.05$ — significance of the difference between groups I and II.

Table 3 — Characteristics of the tone of the ANS in terms of LF/HF ratio

Group	Type of vegetative tone					
	eutonia		vagotonia		sympathicotonia	
	M ± m	n (%)	M ± m	n (%)	M ± m	n (%)
I (n = 15)	1.22 ± 0.36*	2 (13.3)*	0.52 ± 0.08*	11 (73.3)*	5.87 ± 1.18*	2 (13.3)
II (n = 7)	0	0	0.56 ± 0.76*	5 (71.4)*	2.46 ± 0.06*	2 (28.6)
III (n = 3)	2.43 ± 0.11	2 (66.7)	0	1 (33.3)	0	0

Note. * — p < 0.05 — the significance of the difference compared with group III.

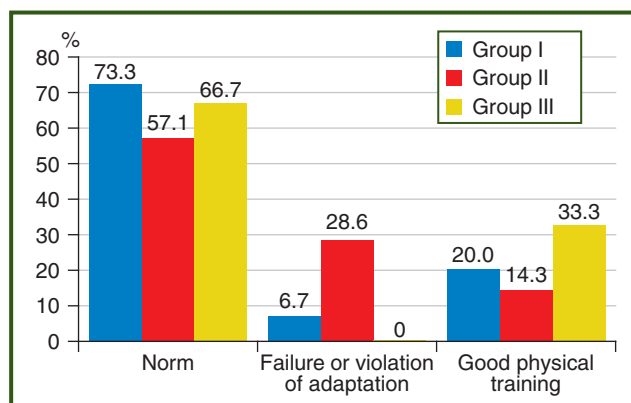


Figure 2 — Distribution of patients according to adaptive potential

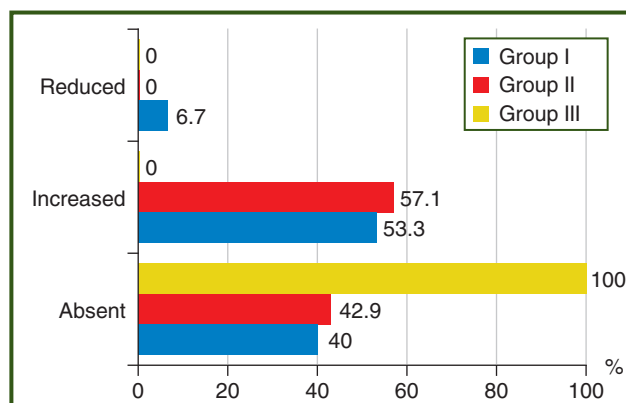


Figure 3 — Distribution of patients by cardiovascular risk

Table 4 — Signs of autonomic dystonia in the examined patients

Indicator	Group I (n = 35)		Group II (n = 22)		Group III (n = 15)	
	n	%	n	%	n	%
Predisposition to any excitement						
— redness of the face	15	42.9	14	63.6	3	20.0
— pale face	4	11.4	3	13.6	2	13.3
Numbness or cooling						
— fingers, toes	16	45.7	15	68.2	7	46.7
— completely hands, feet	1	2.9	3	13.6	2	13.3
Color changes (paleness, redness, cyanosis)						
— fingers, toes	4	11.4	4	18.2	2	13.3
— completely hands, feet	1	2.9	0	0	0	0
Increased sweating	16	45.7	14	63.6	6	40.0
Feeling of palpitations, “fading”, “cardiac arrest”	15	42.9	13	59.1	4	26.7
Feeling of breathing difficulties: shortness of breath, rapid breathing	7	20.0	12	54.6	5	33.3
Indigestion: a tendency to constipation, abdominal bloating, pain	29	82.9	21	95.5	15	100.0
Fainting in a stuffy room, excitement, long stay in an upright position	2	5.7	1	4.6	2	13.3
Paroxysmal headache	17	48.6	8	36.4	3	20.0
Decreased efficiency, rapid fatigue	24	68.6	12	54.6	5	33.3
Sleep disorders						
— difficulty falling asleep	9	25.7	7	31.8	4	26.7
— superficial, light sleep with frequent awakenings	11	31.4	6	27.3	2	13.3
— the feeling of a lack of sleep, fatigue upon awakening in the morning	4	11.4	7	31.8	1	6.7

The analysis of the total spectral power of heart rate variability found that most patients with precancerous conditions of the stomach have a sufficient resource potential. At the same time, in 33.3 % of patients of group I and 28.6 % of group II, depletion of sympathetic and parasympathetic components of ANS was noted.

Evaluation of adaptive capacity in precancerous conditions with comorbidity showed that in most patients the indicators were within normal values. One-third of patients in group III had good physical training, which is 1.7 times higher compared to group I and 2.3 times — compared to group II. At the same time, one-third of people in group II had a failure/violation of adaptation (Fig. 2).

It was found that half of patients with precancerous conditions of the stomach in thyroid comorbidity had an increased cardiovascular risk. At the same time, all patients without thyroid pathology did not have a cardiovascular risk (Fig. 3).

Stress resistance analysis showed that 33.3 % of patients with nodular changes in the thyroid gland and 28.6 % of those with diffuse changes had anxiety syndrome, while among individuals without thyroid pathology anxiety was not detected at all. High stress resistance was observed in 60.0 % of patients of group I, in 71.4 % — of group II and in all patients of group III.

In general, the frequency (83.3 %) of autonomic dysfunction was high in patients with precancerous conditions of the stomach according to the questionnaire of O.M. Vein. The results of the assessment of autonomic dystonia are presented in Table 4, according to which almost all patients most often noted indigestion: a tendency to constipation, abdominal bloating, pain. At the same time, people with nodular changes in the thyroid gland quite often complained of reduced efficiency, rapid fatigue (68.6 %) and sleep disturbances (65.7 %). Patients with diffuse changes in the structure of the thyroid gland often had numbness of the fingers and toes (68.2 %), a tendency to facial redness and increased sweating (63.6 %).

It should be noted that 74.3 % of patients in group I had moderate autonomic disorders — the average score on the scale of O.M. Vein was (29.4 ± 3.6) points, while a pronounced autonomic imbalance occurred in 36.4 % of individuals with diffuse changes in the thyroid gland, which is 1.5 and almost 3 times more often compared to the group with nodular changes in the thyroid gland and people without thyroid pathology (Fig. 4).

According to the results of correlation analysis, it was found that the score on the scale of O.M. Vein directly correlated with the severity of abdominal pain syndrome ($r = 0.53$; $p = 0.030$), diarrheal syndrome ($r = 0.58$; $p = 0.012$), dyspeptic syndrome ($r = 0.44$; $p = 0.029$).

Conclusions

1. Patients with precancerous conditions of the stomach in comorbid pathology of the thyroid gland showed both symptoms of abdominal pain and dyspeptic syndrome, combined with manifestations of reflux.

2. According to Precise system data, half of the patients with precancerous conditions of the stomach with

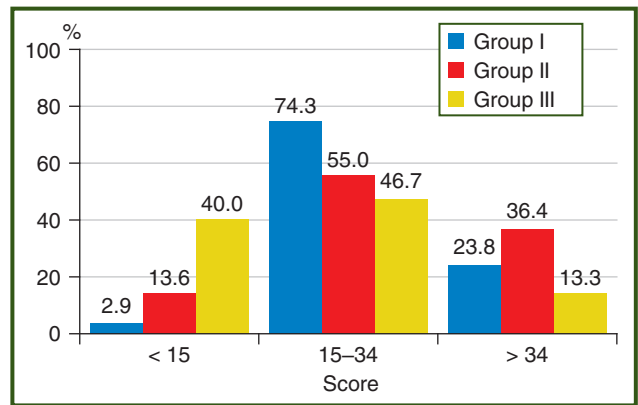


Figure 4 — The severity of autonomic dystonia in the examined patients on the scale of O.M. Wayne

thyroid comorbidity have an increased cardiovascular risk with increased parasympathetic regulation of the autonomic nervous system, and one-third of patients with structural changes in the thyroid gland have a breakdown/maladaptation, anxiety syndrome and exhaustion of the sympathetic and parasympathetic components of the ANS.

3. The correlations between the intensity of clinical syndromes and the severity of autonomic dystonia on Wayne's scale indicate a significant contribution of autonomic disorders in the formation of clinical symptoms in patients with comorbid pathology of the stomach and thyroid gland.

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Contribution of authors: L.M. Mosiychuk — research concept and design, clinical data processing, text editing; O.M. Shevtsova — selection of patients, conducting surveys and diagnosing using Precise system, processing of the obtained data; O.P. Petishko — creation of an electronic database, statistical processing of material, design of the article.

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Клініко-вегетативні порушення, адаптаційні можливості та стресостійкість у хворих на передракові стани шлунка в умовах коморбідності з патологією щитоподібної залози

Резюме. Актуальність. Важливим аспектом перебігу передракових станів шлунка є коморбідність із патологією щитоподібної залози. На сьогодні серед дослідників досі немає єдиної думки щодо участі вегетативної нервової системи у забезпеченні реактивності організму і формуванні адаптаційних процесів у хворих з атрофічним гастритом, поєднаним з тиреоїдитом. **Мета дослідження:** визначити особливості клінічних проявів, вегетативної дисфункції та показників варіабельності серцевого ритму у хворих із передраковими станами шлунка в умовах коморбідної патології щитоподібної залози. **Матеріали та методи.** У дослідження включені 72 пацієнти з хронічним атрофічним гастритом, які були розподілені на 3 групи залежно від змін у структурі щитоподібної залози: I групу становили 35 осіб із вузловими змінами, II — 22 із дифузними, III — 15 осіб без будь-яких змін. Для вивчення клінічної картини в обстежених хворих проведено опитування з використанням Шкали оцінки симптомів з боку шлунково-кишкового тракту. Для виявлення ознак вегетативних порушень використовували опитувальник О.М. Вейна. Оцінку адаптаційних можливостей проводили за допомогою системи Precise на кардіографі CONTEC 8000GW з програмним забезпеченням для аналізу варіабельності серцевого ритму. **Результати.** У пацієнтів із коморбідною патологією найчастіше виявлялися симптоми абдомінального больового синдрому та диспептичного синдрому незалежно від структурних змін щитоподібної залози, а діарейний синдром в I групі відмічали в 1,9 раза рідше порівняно з II групою (p = 0,02) та в 1,8 раза порівняно з III групою (p > 0,05). Встановлено високу частоту

вегетативної дисфункції у хворих із передраковими станами шлунка — 83,3 %. При цьому пацієнти з вузловими змінами в щитоподібній залозі достатньо часто скаржилися на зниження працездатності, швидку втому (68,6 %) та порушення сну (65,7 %). У хворих із дифузними змінами в щитоподібній залозі часто спостерігали оніміння пальців рук, стоп (68,2 %), схильність до почервоіння обличчя та підвищену пітливість (63,6 %). Визначено кореляцію кількості балів за опитувальником О.М. Вейна з інтенсивністю таких синдромів, як абдомінальний біль (r = 0,53; p = 0,030), діарейний синдром (r = 0,58; p = 0,012), диспептичний синдром (r = 0,44; p = 0,029). Аналіз стресостійкості показав, що 33,3 % пацієнтів із вузловими змінами в щитоподібній залозі та 28,6 % із дифузними мали тривожний синдром, у той час як серед осіб без патології щитоподібної залози тривожність не виявлено в жодному випадку. **Висновки.** За даними системи Precise, половина пацієнтів із передраковими станами шлунка в умовах коморбідної патології щитоподібної залози мають підвищений серцево-судинний ризик на фоні збільшення парасимпатичної регуляції вегетативної нервової системи, а третина хворих — зрив/порушення адаптації, тривожний синдром та виснаженість симпатичного та парасимпатичного компонентів вегетативної нервової системи. Виявлені зв'язки свідчать про значний внесок вегетативних порушень у формування клінічної симптоматики в пацієнтів із коморбідною патологією шлунка та щитоподібної залози. **Ключові слова:** вегетативна дисфункція; адаптаційні можливості; стресостійкість; передракові стани шлунка; патологія щитоподібної залози