UDC 616.33-002-007.23-036.1-06:616.441]-073.432.19-037
DOI: 10.14739/2310-1210.2022.3.252716

Ultrasound criteria for predicting pre-cancer changes of the gastric mucosa in patients with chronic atrophic gastritis combined with thyroid pathology

Yu. M. Stepanov[A,F], **L. M. Mosiichuk**[A,E], **I. S. Konenko**[B,C,D], **O. V. Simonova**[B,C,D], **O. P. Petishko***[C,E], **O. M. Shevtsova**[B,C], **L. V. Demeshkina**[B]

State Institution "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Key words: atrophic gastritis, metaplasia, dysplasia, precancerous conditions, ultrasonography.

Zaporozhye medical journal 2022; 24 (3), 286-292

***E-mail:** petishko_oksana@i.ua

Precancerous conditions increase the risk of gastric cancer by 2–3 % every 10 years. Among comorbid pathology, 46 % of all endocrinopathies are diseases of the thyroid gland. An urgent issue today is the definition of non-invasive criteria for the formation of a risk group for the detection of precancerous changes in the gastric mucosa in patients with comorbid pathology.

The aim of the study was to evaluate the structure of the thyroid gland as ultrasound criterion for predicting precancerous lesions in the stomach in patients with atrophic gastritis under conditions of comorbidity.

Materials and methods. The study was conducted among 81 patients with gastric precancerous conditions. The upper endoscopy was performed using EVIS EXERA III systems with an Olympus 190 gastroscope (Japan). All the patients in this study underwent a sonological examination of the thyroid gland on an ultrasound scanner Toshiba Xario (Japan).

Results. In patients with atrophic gastritis, a high frequency of structural changes in the thyroid gland (77 %) was observed. Focal changes were determined in 33 % of atrophic gastritis patients with a predominance of their diagnostic frequency in patients with gastric mucosal dysplasia ($\chi^2 = 5.32$, $P < 0.05$ as compared to the patients with gastric mucosal atrophy and $\chi^2 = 4.25$, $P < 0.05$ as compared to the patients from the intestinal metaplasia group).

Patients with gastric mucosal dysplasia were characterized by coarse-grained thyroid parenchyma, which was more common by 2.2 times as compared to the group of patients with atrophy ($P > 0.05$) and by 1.8 times as compared to the patients with intestinal metaplasia ($\chi^2 = 4.09$, $P < 0.05$).

Conclusions. Diagnostic criteria for the formation of a risk group for the detection of gastric mucosal dysplasia are focal changes in the thyroid parenchyma (sensitivity 63.6 %, specificity 71.4 %), coarse granularity of the thyroid parenchyma (sensitivity 72.7 %, specificity 61.4 %) and an increased vascularization of parenchyma at the sonological examination of the thyroid gland (sensitivity 63.6 %, specificity 70.0 %).

Ключові слова: атрофічний гастрит, метаплазія, дисплазія, захворювання щитовидної залози, передракові захворювання, ультрасонографія.

Запорізький медичний журнал. 2022. Т. 24, № 3(132). С. 286-292

Ультразвукові критерії прогнозування передракових змін слизової оболонки шлунка у хворих на хронічний атрофічний гастрит, поєднаний із патологією щитовидної залози

Ю. М. Степанов, Л. М. Мосійчук, І. С. Коненко, О. В. Сімонова, О. П. Петішко, О. М. Шевцова, Л. В. Демешкіна

Передракові стані зумовлюють зростання ризику розвитку раку шлунка на 2–3 % кожні 10 років. Серед коморбідних патологій 46 % від усіх ендокринопатій становлять захворювання щитовидної залози. Актуальним питанням залишається визначення неінвазивних критеріїв формування групи ризику виявлення передракових змін слизової оболонки шлунка у хворих із коморбідною патологією.

Мета роботи – оцінювання показників структури щитовидної залози як ультразвукових критеріїв прогнозування передракових змін шлунка у хворих на атрофічний гастрит в умовах коморбідності.

Матеріали та методи. Дослідження здійснили у 81 хворого з передраковими станами шлунка. Верхню ендоскопію виконали, використавши систему EVIS EXERA III з гастроскопом Olympus 190 (Японія). Всім обстеженим здійснили сонологічне дослідження щитовидної залози на ультразвуковому сканері Toshiba Xario (Japan).

Результати. У хворих на атрофічний гастрит виявили високу частоту структурних змін щитовидної залози (77 %). Вогнищеві зміни визначали у 33 % хворих на хронічний атрофічний гастрит, переважно в пацієнтів із дисплазією слизової оболонки шлунка ($\chi^2 = 5,32$, $p < 0,05$ порівняно з пацієнтами з атрофією слизової оболонки шлунка; $\chi^2 = 4,25$, $p < 0,05$ щодо показника хворих із групи кишкової метаплазії).

Для пацієнтів із дисплазією слизової оболонки шлунка характерна крупнозерниста паренхіма щитовидної залози, яку виявляли в 2,2 раза частіше порівняно з групою осіб з атрофією ($p > 0,05$), в 1,8 раза частіше щодо пацієнтів із кишковою метаплазією ($\chi^2 = 4,09$, $p < 0,05$).

Висновки. Діагностичні критерії формування групи ризику виявлення дисплазії слизової оболонки шлунка – вогнищеві зміни паренхіми щитовидної залози (чутливість 63,6 %, специфічність 71,4 %), велика зернистість паренхіми щитовидної залози (чутливість 72,7 %, специфічність 61,4 %) та посилена васкуляризація паренхіми під час сонологічного дослідження щитовидної залози (чутливість 63,6 %, специфічність 70,0 %).

More than half of the people worldwide suffer from chronic gastritis accompanied by the prolonged inflammation that results in the destruction of the gastric mucosa (GM) with the loss of gastric glands – the formation of atrophic gastritis [1,2]. In atrophic gastritis, in its turn, there is a high risk of restructuring changes in the form of replacement of the lost glands with new immature ones, similar in their structure to small or large intestinal glands – the so-called elements of intestinal metaplasia, and the risk of losing the cell architecture, i. e. dysplastic changes, and as a consequence, the emergence of gastric cancer [3,4]. It is known that such processes last quite long, but the severe socio-economic consequences of such a disease as gastric cancer necessitate search for markers of timely detection and prediction of precancerous structural changes in the stomach [5].

According to the European guidelines "Management of epithelial precancerous conditions and lesions in the stomach (MAPS II)" (2019), precancerous conditions and precancerous lesions are distinguished in the stomach among precancers [6]. The former include diseases that cause a significant increase in the cancer risk, the latter – morphological changes in the tissue, in which cancer can occur more likely than in the normal tissue. Therefore, GM atrophy and intestinal metaplasia (IM), according to the MAPS consensus, are precancerous conditions. GM dysplasia is the penultimate stage in the progression of gastric carcinogenesis that refers to precancerous lesions and therefore is a direct precancerous damage of the GM [7].

Precancerous conditions increase the risk of gastric cancer by 2–3 % every 10 years, including the atrophic gastritis – by 0.8 %, intestinal metaplasia – by 1.8 %, mild and moderate dysplasia – by 3.9 % and severe dysplasia – by 32.7 % [8].

The use of modern endoscopic diagnostic methods (video endoscopy with high resolution, magnification and narrow-band imaging) allows with a high probability to diagnose precancerous conditions of the stomach, to perform a highly precise tissue sampling (targeted biopsy) [9,10]. However, endoscopy is an invasive method that has its limitations, especially among the elderly, who often have a comorbid pathology. In addition, precancerous changes in GM and cancer are diagnosed at a late stage mostly among this category of patients.

Among comorbid pathologies, an endocrine pathology occurs quite often, with 46 % of all endocrinopathies being the diseases of the thyroid gland (TG) [11]. The most common pathology is diffuse and nodular goiters. Their level in the western regions of Ukraine is higher than the national average levels and the levels in the north-eastern regions [12]. According to O. O. Chukur, in 5 years (2013–2017), the incidence of hypothyroidism increased by 28.4 %, hyperthyroidism/thyrotoxicosis – by 8 %, and the prevalence of thyroiditis increased by 12.7 % [13]. Moreover, according to the Health Ministry of Ukraine, up to 80 % of elderly people suffer from TG pathology [11]. According to experts, the upward tendency in the number of thyroid diseases will remain in the coming years due to nutritional disorders, genetic predisposition, adverse environmental conditions [14].

Screening of patients having autoimmune TG diseases with the help of pepsinogen I and I/II has enabled to reveal autoimmune gastritis with oxyntic gastric atrophy and can be recommended for the prevention of gastric cancer [15].

2D-mode with color-Doppler ultrasound of TG is the most useful imaging method to differentiate between normal TG parenchyma and diffuse or nodular lesions by assessing the size, echogenicity, echostructure and vascularization [16–18].

The non-invasiveness and safety of the sonological method have contributed to its widespread introduction as a screening method for all age groups of patients. Given that there are studies showing a fairly high percentage of random detection of TG structural changes in patients with atrophic gastritis, as well as a significant increase in the frequency of GM structural changes in patients with thyroid disease, it is topical to determine the criteria of risk for precancerous states development in patients with comorbid pathology.

Aim

The aim of the study was to evaluate the structure of the TG as ultrasound criterion for predicting precancerous lesions in the stomach among patients with atrophic gastritis under conditions of comorbidity.

Materials and methods

The study included 81 patients with precancerous gastric conditions. Among the examined patients, there were 56 (69.1 %) women and 25 (30.9 %) men aged from 32 to 76 years, the mean age was 58.3 ± 1.5 years. The upper endoscopy was performed using EVIS EXERA III systems with an Olympus 190 gastroscope (Japan). When using the function of near-focus narrow-band imaging, the presence of GM atrophy was determined by the disappearance of the capillary subepithelial network pattern with randomly arranged collecting venules. The prevalence of GM atrophic changes (in the antrum, body and diffuse) was determined. Diagnosis of intestinal metaplasia (IM) was performed by detecting flat-raised and flat-deepened foci, which in the mode of magnification had a regular comb-like or tubulovillous microstructure. The presence of deformed GM microvascular pattern and the irregular microstructure indicated dysplasia [2]. In all cases, a morphological verification of the lesions detected during endoscopic examination was performed according to OLGA and OLGIM standards.

All the patients in the study underwent a sonological examination of the TG on an ultrasound scanner Toshiba Xario (Japan) using a multifrequency linear transducer with a frequency of 5–12 MHz. The B-mode, the color and energy Doppler were used to analyze the structural characteristics of the TG.

All patients signed an informed consent to participate in this study.

The obtained results were statistically analyzed using the application package Statistica 6.1. The chi-square criterion with Yates's correction (χ^2) was used to compare the distribution of qualitative data. The statistical significance of the difference was estimated at the level not lower than 95.0 % ($P < 0.05$). Diagnostic significance of the indicators was evaluated by determining the sensitivity, specificity, diagnostic accuracy, as well as by calculating the odds ratio (OR) and its statistical significance.

Results

According to the results of endoscopic examination, all patients were diagnosed with GM atrophy (*Figs. 1, 2*), the frequency of atrophy limited to the antrum and diffuse atrophic changes in GM was almost the same (58 % and 42 %, respectively). Video endoscopy allowed to diagnose IM with high probability in 69 patients with GM atrophy (*Fig. 3*). The study of the IM prevalence in the stomach showed a 1.5-fold increase in frequency of its diffuse pattern, which is a significant indicator of the structural progressive changes in the precancerous direction. GM dysplasia was detected only in 11 patients with chronic atrophic gastritis (CAG), which was observed with IM (*Fig. 4*). In general, structural changes of the thyroid parenchyma were detected in 62 (77 %) of the examined patients. Diffuse changes were most often diagnosed – 50 (62 %) cases (*Fig. 5*).

One third of the examined patients were diagnosed with thyroid hyperplasia and only in two cases – with thyroid hypoplasia. Ultrasound changes characteristic of thyroiditis were detected in isolated cases; changes characteristic of chronic autoimmune thyroiditis were observed twice more often in patients with GM dysplasia than those in patients with IM ($\chi^2 = 4.80$, $P < 0.05$), the location of the TG in all cases was typical, without changes in the shadow of the trachea. An increase in the thyroid volume was detected only in 3 cases.

A further comparative analysis of thyroid ultrasound data was performed in 12 patients with GM atrophy alone, 58 patients with IM and atrophy and in 11 patients with GM dysplasia (*Table 1*).

As it can be seen from the table, the frequency of TG diffuse changes was the highest in patients with GM dysplasia, which was 1.8 and 1.6 times higher than in patients with atrophic GM changes alone and patients with IM ($\chi^2 = 4.54$, $P < 0.05$ and $\chi^2 = 4.17$, $P < 0.05$, respectively).

Focal changes were determined in 33 % of CAG patients with a predominance of their diagnostic frequency in patients with GM dysplasia ($\chi^2 = 5.32$, $P < 0.05$ as compared to the patients with GM atrophy and ($\chi^2 = 4.25$, $P < 0.05$ as compared to the patients from the IM group).

Fig. 6 shows the Doppler image of the TG left lobe in a patient with GM dysplasia.

28 % of patients with IM and 36 % of patients with GM dysplasia presented a pathological indicator of the thyroid contour in the form of its roughness. Fuzzy contour visualization was diagnosed in one case among patients with GM atrophy, in 34 % of patients with IM and in 46 % of the examined patients with dysplastic GM changes.

A dense thyroid capsule was detected in 82 % of patients with GM dysplasia, which was 2.5 times more often than in patients with GM atrophy ($\chi^2 = 5.49$, $P < 0.05$) and 1.5 times ($P > 0.05$) – in comparison to patients with IM (*Table 2*).

With the development of IM and GM dysplasia, the detection frequency of fibrous strands in the TG were 3 times increased, indicating a long course of the inflammatory process in the gland. Changes in thyroid echogenicity were observed in 35 % of patients. In most cases, changes in the gland parenchyma echogenicity were manifested by its increase, and reduced echogenicity of the TG was detected only in 3 cases among patients with GM dysplasia.

Patients with atrophic GM changes alone and IM were more likely to have fine-grained parenchyma, while patients with GM dysplasia were characterized by coarse-grained thyroid parenchyma, which was 2.2 times more common as compared to the group of patients with atrophy ($P > 0.05$) and 1.8 times – as compared to patients with IM ($\chi^2 = 4.09$, $P < 0.05$).

Signs of lymphadenopathy were observed in only two patients with GM dysplasia.

To form a risk group for dysplastic GM changes, the informativeness of thyroid sonological parameters was assessed and it was found that the risk of detecting precancerous structural changes in GM was 4.38 times increased in the presence of focal changes in the TG (*Table 3*).

Also, the large granularity and increased vascularization of the thyroid parenchyma, detected during the ultrasound examination, quadruple the risk of GM dysplasia in patients with CAG in the condition of comorbidity with thyroid pathology.

Table 1. The detection frequency of TG ultrasound and clinical changes in CAG patients

Clinical and ultrasound characteristics of TG	Patients with GM atrophy (n = 12)		Patients with IM and GM atrophy (n = 58)		Patients with GM dysplasia (n = 11)	
	n	%	n	%	n	%
Thyroid hypoplasia	0	0	0	0	2	18
Thyroid hyperplasia	4	33	19	33	6	30
Thyroid without structural changes	5	42	13	22	1	9
Diffuse thyroid changes	6	50*	34	59*	10	91
Focal changes of the thyroid gland	2	17*	18	31*	7	64
Thyroiditis	0	0	0	0	2	18
Chronic autoimmune thyroiditis	0	0	17	29*	7	64

*: $P < 0.05$ – a significant difference as compared to patients with GM dysplasia.

Table 2. Frequency of structural changes of the thyroid parenchyma in the examined patients

Indicators of structural changes	Patients with GM atrophy (n = 12)		Patients with IM and GM atrophy (n = 58)		Patients with GM dysplasia (n = 11)	
	n	%	n	%	n	%
Dense thyroid capsule	4	33	31	53	9	82*
Heterogeneous structure of the parenchyma:	7	58	46	79	11	100*
– fibrous strands	1	8	22	38*	4	36
– areas of reduced echogenicity	3	25	24	41	5	46
– follicles	4	33	22	38	8	73#
Parenchyma granularity:						
– fine	8	67	35	60	3	27
– coarse	4	33	23	40	8	73#
Echogenicity:						
– normal	9	75	40	69	4	36
– reduced	0	0	0	0	3	28
– increased	3	25	18	31	4	36

*: $P < 0.05$ – a significant difference as compared to patients with GM atrophy alone; #: $P < 0.05$ – a significant difference as compared to patients with gastric IM.

Table 3. Characteristics of TG sonological data as diagnostic criteria for the formation of the risk group for dysplastic GM changes in patients with CAG

Indicator	Odds Ratio (OR)	Sensitivity, %	Specificity, %	Diagnostic accuracy, %	Significance
Focal changes in the TG	4.38 (1.15; 16.60)	63.6	71.4	70.4	0.036
Coarse granularity of the thyroid parenchyma	4.25 (1.04; 17.42)	72.7	61.4	63.0	0.049
Enhanced vascularization	4.08 (1.08; 15.45)	63.6	70.0	69.1	0.042

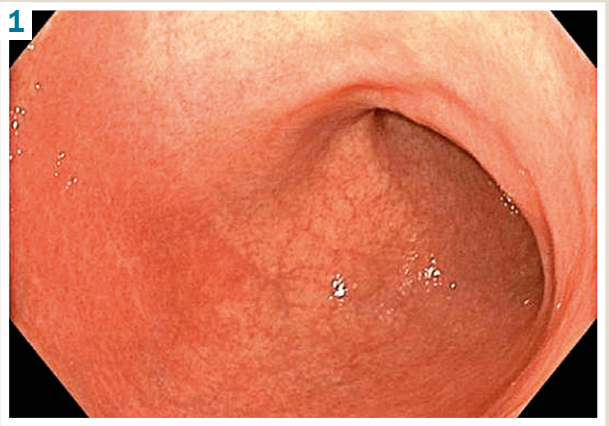
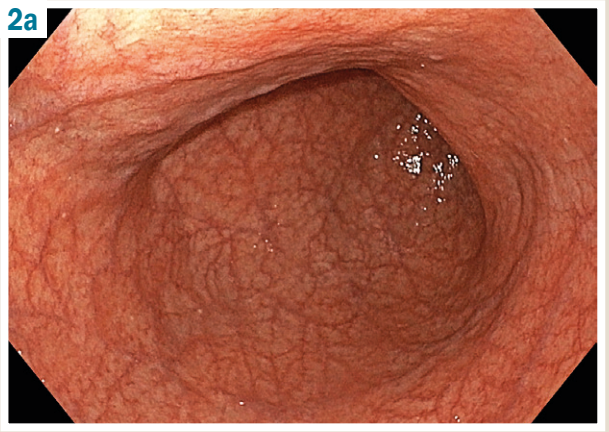


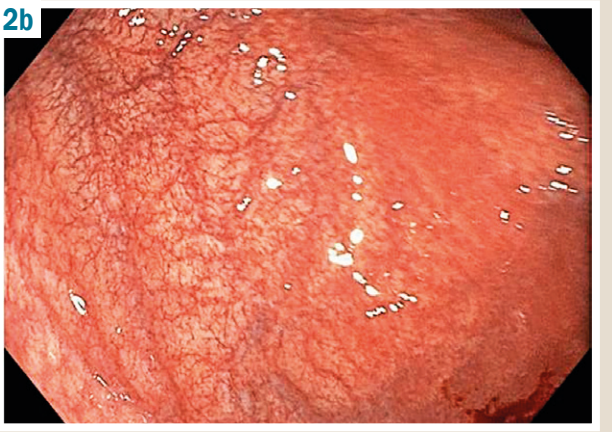
Fig. 1. Patient O. GM atrophy of the antrum.

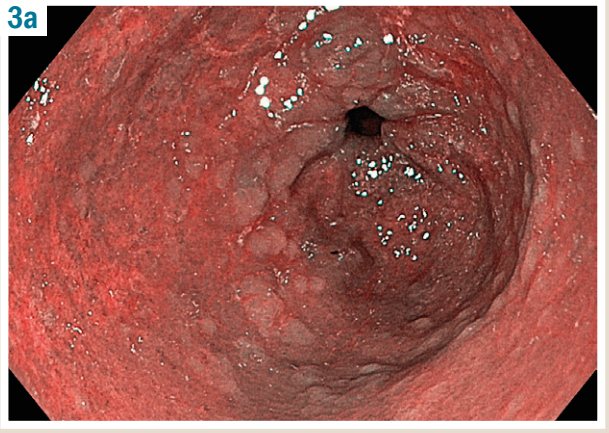
Fig. 2. Patient S. Diffuse GM atrophy.

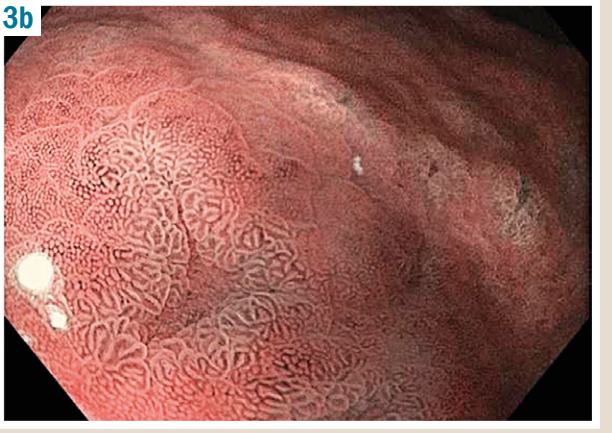
Fig. 3. Patient K. IM of the GM. An NBI-mode examination.

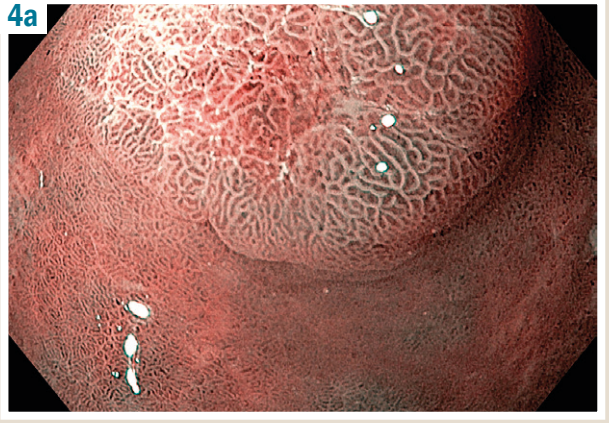
Fig. 4. GM dysplasia in the polypoid mass of the prepyloric area in patient H. (**4a**); GM dysplasia in the gastric body in patient M. (**4b**).

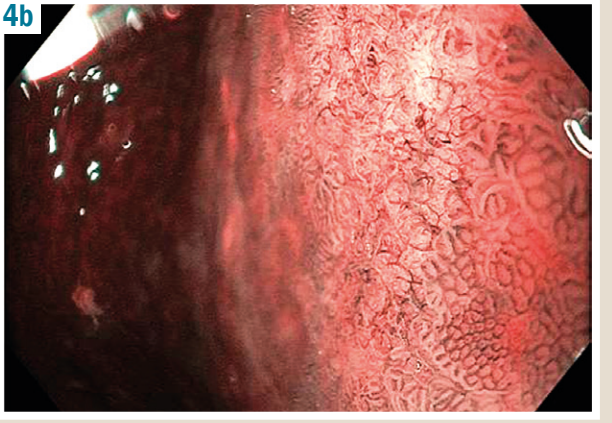












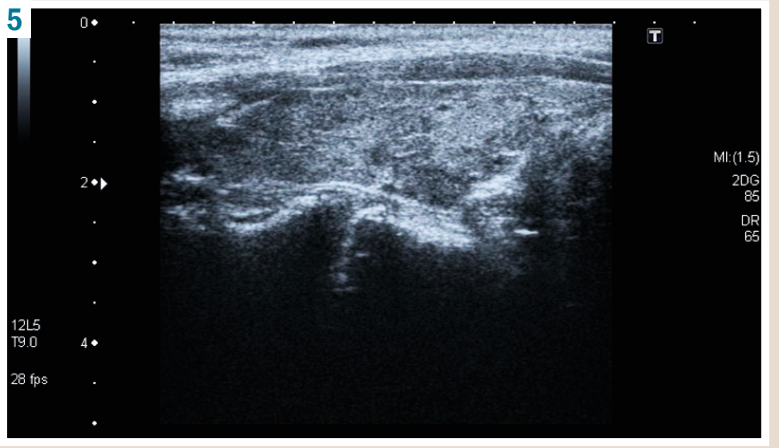
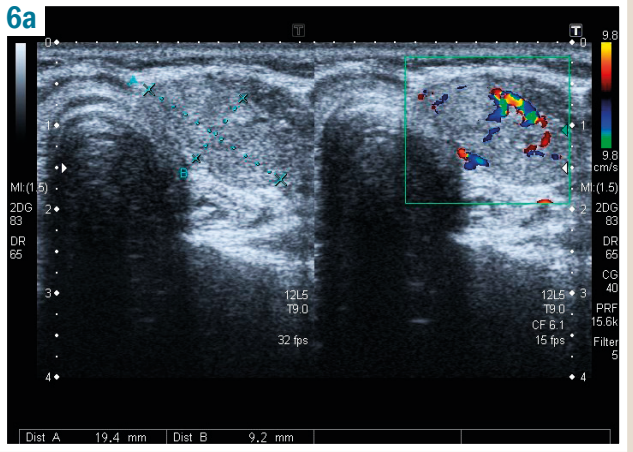


Fig. 5. Diffuse changes of the thyroid parenchyma in patient S. with GM atrophy.



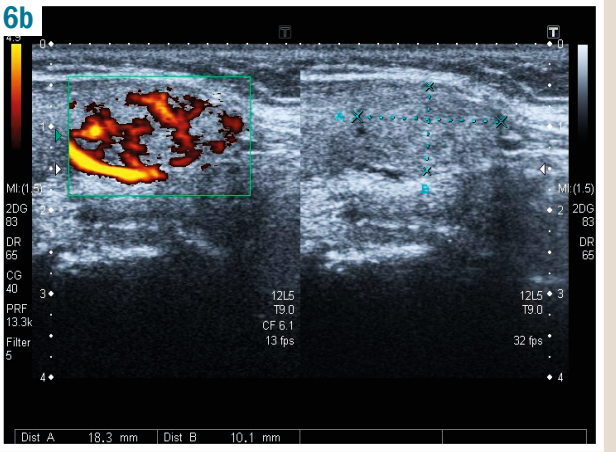


Fig. 6. Dopplerogram in the color and energy regime of the node in the TG left lobe in patient K. with GM dysplasia.

Discussion

Thus, the results of the study confirm the well-known fact of a close interrelation between the stomach and thyroid diseases. It is the presence of structural changes of precancerous character in GM that are associated with structural changes of the TG in 77 % of cases, according to our data. Similar data obtained from an examination of a large group of adults and presented by E. G. Kandemir and co-authors, C. C. Abnet and co-authors showed a significantly high level of association between nodular goiter and gastric non-cardiac adenocarcinoma [19,20].

In a review, A. R. Brown and colleagues refer to several hypotheses that could explain such results. The first hypothesis is based on the common embryogenesis of the stomach and TG (theory of the Italian scientist S. Ventiru), as a result of which an iodine deficiency causes the development of gastritis with the subsequent possible development of adenocarcinoma. The second hypothesis is based on the properties of iodine, which provide protection against gastric adenocarcinoma, acting as an antioxidant in its mucosa [21]. However, currently, there are no complete answers to these questions.

Therefore, the data obtained indicate the reasonability of endoscopic examination of the stomach in patients with thyroid pathology, especially of focal nature. And vice versa, it is reasonable to send patients with CAG diagnosis to undergo a sonological examination of the TG.

Conclusions

1. In patients with CAG, a high frequency of structural changes in the thyroid gland (77 %) is observed.

2. The frequency of structural changes in the thyroid gland increases as the restructuring changes in the stomach deepen.

3. Diagnostic criteria for the risk group formation to detect GM dysplasia are focal changes in the thyroid parenchyma (sensitivity 63.6 %, specificity 71.4 %), coarse granularity of the thyroid parenchyma (sensitivity 72.7 %, specificity 61.4 %) and increased vascularization of parenchyma on the sonological examination of the thyroid gland (sensitivity 63.6 %, specificity 70.0 %).

Prospects for further research. We consider the substantiation of new approaches to tactics of management for patients with precancerous conditions of the stomach in the conditions of comorbidity as a perspective and important scientific direction.

Funding

The work is performed in accordance with the research plan of the State Institution "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine" in the research work "To study the features of comorbid status and cytokine balance in patients with precancerous gastric conditions and justify new approaches to diagnostic and treatment tactics", state registration No. 0118U001833.

Conflicts of interest: authors have no conflict of interest to declare.
Конфлікт інтересів: відсутній.

Надійшла до редакції / Received: 10.02.2022
Після доопрацювання / Revised: 23.02.2022
Прийнято до друку / Accepted: 17.03.2022

Information about authors:
Stepanov Yu. M., MD, PhD, DSc, Professor, Corresponding Member of the NAMS of Ukraine, Director of SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro.
ORCID ID: 0000-0002-6721-2468
Mosiichuk L. M., MD, PhD, DSc, Senior Researcher, Head of the Department of Diseases of the Stomach and Duodenum, Dietetics and Medical Nutrition, SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro.
ORCID ID: 0000-0001-9296-9473
Konenko I. S., MD, PhD, Senior Researcher of the Department of Mini-invasive Endoscopic Interventions and Instrumental Diagnostics, SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro.
ORCID ID: 0000-0002-7619-699X
Simonova O. V., MD, PhD, Senior Researcher of the Department of Mini-invasive Endoscopic Interventions and Instrumental Diagnostics, SI «Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine», Dnipro.
ORCID ID: 0000-0001-7954-1333
Petishko O. P., Researcher of the Department of Scientific-Organizational, Methodical Work and Information Technologies, SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro.
ORCID ID: 0000-0002-4559-4055
Shevtsova O. M., Junior Researcher of the Department of Diseases of the Stomach and Duodenum, Dietetics and Medical Nutrition, SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro.
ORCID ID: 0000-0002-9752-5983
Demeshkina L. V., MD, PhD, Senior Researcher of the Department of Diseases of the Stomach and Duodenum, Dietetics and Medical Nutrition, SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Dnipro.
ORCID ID: 0000-0002-7301-1857

Відомості про авторів:
Степанов Ю. М., член-кор. НАМН України, д-р мед. наук, професор, директор ДУ «Інститут гастроентерології НАМН України», м. Дніпро.
Мосійчук Л. М., д-р мед. наук, старший науковий співробітник, зав. відділу захворювань шлунка та дванадцятипалої кишки, дієтології і лікувального харчування, ДУ «Інститут гастроентерології НАМН України», м. Дніпро.
Коненко І. С., канд. мед. наук, старший науковий співробітник відділу мініінвазивних ендоскопічних втручань та інструментальної діагностики, ДУ «Інститут гастроентерології НАМН України», м. Дніпро.
Сімонова О. В., канд. мед. наук, старший науковий співробітник відділу мініінвазивних ендоскопічних втручань та інструментальної діагностики, ДУ «Інститут гастроентерології НАМН України», м. Дніпро.
Петішко О. П., науковий співробітник відділу науково-організаційної, методичної роботи та інформаційних технологій, ДУ «Інститут гастроентерології НАМН України», м. Дніпро.
Шевцова О. М., молодший науковий співробітник відділу захворювань шлунка та дванадцятипалої кишки, дієтології і лікувального харчування, ДУ «Інститут гастроентерології НАМН України», м. Дніпро.
Демешкіна Л. В., канд. мед. наук, старший науковий співробітник відділу захворювань шлунка та дванадцятипалої кишки, дієтології і лікувального харчування, ДУ «Інститут гастроентерології НАМН України», м. Дніпро.

References

[1] Annibale, B., Esposito, G., & Lahner, E. (2020). A current clinical overview of atrophic gastritis. *Expert Review of Gastroenterology & Hepatology, 14*(2), 93-102. https://doi.org/10.1080/17474124.2020.1718491
[2] Lahner, E., Zagari, R. M., Zullo, A., Di Sabatino, A., Meggio, A., Cesaro, P., Lenti, M. V., Annibale, B., & Corazza, G. R. (2019). Chronic atrophic gastritis: Natural history, diagnosis and therapeutic management. A position paper by the Italian Society of Hospital Gastroenterologists and Digestive Endoscopists [AIGO], the Italian Society of Digestive Endoscopy [SIED], the Italian Society of Gastroenterology [SIGE], and the Italian Society of Internal Medicine [SIMI]. *Digestive and Liver Disease, 51*(12), 1621-1632. https://doi.org/10.1016/j.dld.2019.09.016
[3] Kim, Y. J., Lee, S. Y., Yang, H., Kim, J. H., Sung, I. K., & Park, H. S. (2019). Nodular Gastritis as a Precursor Lesion of Atrophic and Metaplastic Gastritis. *Korean Journal of Gastroenterology, 73*(6), 332-340. https://doi.org/10.4166/kjg.2019.73.6.332
[4] Yoon, K., & Kim, N. (2018). Reversibility of Atrophic Gastritis and Intestinal Metaplasia by Eradication of Helicobacter pylori. *Korean Journal of Gastroenterology, 72*(3), 104-115. https://doi.org/10.4166/kjg.2018.72.3.104
[5] Vannella, L., Lahner, E., & Annibale, B. (2012). Risk for gastric neoplasias in patients with chronic atrophic gastritis: a critical reappraisal. *World Journal of Gastroenterology, 18*(12), 1279-1285. https://doi.org/10.3748/wjg.v18.i12.1279
[6] Pimentel-Nunes, P., Libânio, D., Marcos-Pinto, R., Areia, M., Leja, M., Esposito, G., Garrido, M., Kikuste, I., Megraud, F., Matysiak-Budnik, T., Annibale, B., Dumonceau, J. M., Barros, R., Fléjou, J. F., Carneiro, F., van Hooft, J. E., Kuipers, E. J., & Dinis-Ribeiro, M. (2019). Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy, 51*(4), 365-388. https://doi.org/10.1055/a-0859-1883
[7] Correa, P., & Piazuelo, M. B. (2012). The gastric precancerous cascade. *Journal of Digestive Diseases, 13*(1), 2-9. https://doi.org/10.1111/j.1751-2980.2011.00550.x
[8] Sugano, K., Tack, J., Kuipers, E. J., Graham, D. Y., El-Omar, E. M., Miura, S., Haruma, K., Asaka, M., Uemura, N., Malfertheiner, P., & faculty members of Kyoto Global Consensus Conference. (2015). Kyoto global consensus report on Helicobacter pylori gastritis. *Gut, 64*(9), 1353-1367. https://doi.org/10.1136/gutjnl-2015-309252
[9] Zhou, F., Wu, L., Huang, M., Jin, Q., Qin, Y., & Chen, J. (2018). The accuracy of magnifying narrow band imaging (ME-NBI) in distinguishing between cancerous and noncancerous gastric lesions: A meta-analysis. *Medicine, 97*(9), Article e9780. https://doi.org/10.1097/MD.0000000000009780
[10] Boscolo Nata, F., Tirelli, G., Capriotti, V., Marcuzzo, A. V., Sacchet, E., Šuran-Brunelli, A. N., & de Manzini, N. (2021). NBI utility in oncologic surgery: An organ by organ review. *Surgical Oncology, 36*, 65-75. https://doi.org/10.1016/j.suronc.2020.11.017
[11] Kamyshna, I. I., Pavlovich, L. B., Maslyanko, V. A., & Chornenka, Zh. A. (2021). Epidemiological assessment of dymamics of the prevalence and incidence of the thyroid gland diseases in Ukraine and chernivtsi region. *Clinical and experimental pathology, 20*(3), 75-81. https://doi.org/10.24061/1727-4338.XX.3.77.2021.11
[12] Skrypnyk, N. V., & Marusyn, O. V. (2017). Dynamika zakhvoriuvanosti y poshyrenosti vuzlovykh utvoren shchytopodibnoi zalozy za desiatyrichnyi period (2006-2016 rr.) v Ukraini ta na Prykarpatti [Dynamics of incidence and prevalence of thyroid gland nodules in Ukraine and in the Carpathian region for ten years (2006-2016)]. *Praktykuiuchyi likar, 6*(2), 26-29. [in Ukrainian].
[13] Chukur, O. O. (2018). Dynamika zakhvoriuvanosti y poshyrenosti patolohii shchytopodibnoi zalozy sered dorosloho naselennia Ukrainy [Dynamics of morbidity and expansion of pathology of the thyroid gland among adult population of Ukraine]. *Visnyk sotsialnoi hihiieny ta orhanizatsii okhorony zdorovia Ukrainy*, (4), 19-25. https://doi.org/10.11603/1681-2786.2018.4.10020 [in Ukrainian].
[14] Tkachenko, V. I., Maksymets, Ya. A., Vydyborets, N. V., & Kovalenko, O. F. (2018). Analiz poshyrenosti tyreoidnoi patolohii ta zakhvoriuvanosti na nei sered naselennia Kyivskoi oblasti ta Ukrainy za 2007-2017 rr. [Analysis of the prevalence and morbidity of thyroid pathology among the population of Kyiv region and Ukraine for 2007-2017]. *Mižnarodnij endokrinologičnij žurnal, 14*(3), 279-284. https://doi.org/10.22141/2224-0721.14.3.2018.136426 [in Ukrainian].
[15] Venerito, M., Link, A., Rokkas, T., & Malfertheiner, P. (2016). Gastric cancer – clinical and epidemiological aspects. *Helicobacter, 21*(S1), 39-44. https://doi.org/10.1111/hel.12339
[16] Dobruch-Sobczak, K., Jędrzejowski, M., Jakubowski, W., & Trzebińska, A. (2014). Errors and mistakes in ultrasound diagnostics of

the thyroid gland. *Journal of Ultrasonography, 14*(56), 61-73. https://doi.org/10.15557/JoU.2014.0006

[17] Gajda, S. N., Kuryłowicz, A., Żach, M., Bednarczuk, T., & Wyleżoł, M. (2019). Diagnosis and treatment of thyroid disorders in obese patients – what do we know? *Endokrynologia Polska, 70*(3), 271-276. https://doi.org/10.5603/EP.a2018.0089

[18] Alexander, L. F., Patel, N. J., Caserta, M. P., & Robbin, M. L. (2020). Thyroid Ultrasound: Diffuse and Nodular Disease. *Radiologic Clinics of North America, 58*(6), 1041-1057. https://doi.org/10.1016/j.rcl.2020.07.003

[19] Kandemir, E. G., Yonem, A., & Narin, Y. (2005). Gastric Carcinoma and Thyroid Status. *Journal of International Medical Research, 33*(2), 222-227. https://doi.org/10.1177/147323000503300210

[20] Abnet, C. C., Fan, J. H., Kamangar, F., Sun, X. D., Taylor, P. R., Ren, J. S., Mark, S. D., Zhao, P., Fraumeni, J. F., Jr, Qiao, Y. L., & Dawsey, S. M. (2006). Self-reported goiter is associated with a significantly increased risk of gastric noncardia adenocarcinoma in a large population-based Chinese cohort. *International Journal of Cancer, 119*(6), 1508-1510. https://doi.org/10.1002/ijc.21993

[21] Brown, A. R., Simmen, R. C., & Simmen, F. A. (2013). The Role of Thyroid Hormone Signaling in the Prevention of Digestive System Cancers. *International Journal of Molecular Sciences, 14*(8), 16240-16257. https://doi.org/10.3390/ijms140816240