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


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:
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- metaplasia,
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- precancerous conditions,
- ultrasonography.

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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 detected 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 %).

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 стани 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 сьогодення є визначення непідроздільних 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 здійснено на 81 хворому з передраковими станами шлунка. Верхньою ендоскопією виконали використання систему EVIS EXERA III з гастроскопом Olympus 190 (Японія). Всім обстеженим здійснили сонологічне оцінювання показників структури щитовидної залози: $\chi^2 = 5.32, P < 0.05$ порівняно з пацієнтами з атрофією слизової оболонки шлунка; $\chi^2 = 4.25, P < 0.05$, щодо показника впливу слизової оболонки на ультразвуковому сканері Toshiba Xario (Японія). Всім обстеженим здійснили сонологічне оцінювання показників структури щитовидної залози: $\chi^2 = 4.25, P < 0.05$ щодо показника впливу слизової оболонки на ультразвуковому сканері Toshiba Xario (Японія). Всім обстеженим здійснили сонологічне оцінювання показників структури щитовидної залози: $\chi^2 = 4.09, P < 0.05$.

Результати. У хворих на атрофічний гастрит виявили високу частоту структурних змін щитовидної залози (77 %). Вони виявлялися у 33 % хворих на хронічний атрофічний гастрит, переважно в пацієнтів з інтенсивною сосудисто-венивою дисплазією 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 впливу слизової оболонки на ультразвуковому сканері Toshiba Xario (Японія). У хворих з коморбідною патологією ці показники були відомі на рівні $\chi^2 = 4.09, P < 0.05$.

Висновки. Діагностичні критерії формування групи ризику виявлення дисплазії слизової оболонки шлунка – вони виявлення високих чутливість 63,6 %, специфічність 71,4 %, велика зміна слизової оболонки 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/hyperthyrotoxicosis – 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].

The obtained results were statistically analyzed using the application package Statistica 6.1. The chi-square criterion with Yates’s correction ($\chi^2$) 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 ($\chi^2 = 5.32, P < 0.05$ 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).

Table 3 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 coarse-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

<table>
<thead>
<tr>
<th>Clinical and ultrasound characteristics of TG</th>
<th>Patients with GM atrophy (n = 12)</th>
<th>Patients with IM and GM atrophy (n = 58)</th>
<th>Patients with GM dysplasia (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid hypoplasia</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid hyperplasia</td>
<td>4</td>
<td>33</td>
<td>19</td>
</tr>
<tr>
<td>Thyroid without structural changes</td>
<td>5</td>
<td>42</td>
<td>13</td>
</tr>
<tr>
<td>Diffuse thyroid changes</td>
<td>6</td>
<td>50*</td>
<td>34</td>
</tr>
<tr>
<td>Focal changes of the thyroid gland</td>
<td>2</td>
<td>17*</td>
<td>18</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chronic autoimmune thyroiditis</td>
<td>0</td>
<td>0</td>
<td>17*</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Indicators of structural changes</th>
<th>Patients with GM atrophy (n = 12)</th>
<th>Patients with IM and GM atrophy (n = 58)</th>
<th>Patients with GM dysplasia (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dense thyroid capsule</td>
<td>4</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>Heterogeneous structure of the parenchyma:</td>
<td>7</td>
<td>58</td>
<td>46</td>
</tr>
<tr>
<td>– fibrous strands</td>
<td>1</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>– areas of reduced echogenicity</td>
<td>3</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>– follicles</td>
<td>4</td>
<td>33</td>
<td>22</td>
</tr>
<tr>
<td>Parenchyma granularity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– fine</td>
<td>8</td>
<td>67</td>
<td>35</td>
</tr>
<tr>
<td>– coarse</td>
<td>4</td>
<td>33</td>
<td>23</td>
</tr>
<tr>
<td>Echogenicity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– normal</td>
<td>9</td>
<td>75</td>
<td>40</td>
</tr>
<tr>
<td>– reduced</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>– increased</td>
<td>3</td>
<td>25</td>
<td>18</td>
</tr>
</tbody>
</table>

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

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

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