

**LESIONS OF THE GASTRO-DUODENAL ZONE AND THEIR RELATIONSHIP WITH
CLINICAL AND ANGIOGRAPHIC DATA IN PATIENTS WITH ISCHEMIC HEART
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SUMMARY

Purpose: analysis of lesions of the gastroduodenal zone in relation to angiographic and clinical laboratory parameters in patients with coronary artery disease (CAD). **Material and methods:** In the period from 03/01/2021 to 09/01/2021, 298 patients with CAD were examined, who underwent coronary angiography (CAG) and percutaneous coronary intervention (PCI) with stenting. In addition to general clinical laboratory and functional research methods, esophagogastroduodenoscopy (EGDS) was carried out in order to assess the localization and nature of lesions of the gastroduodenal zone (GDZ). **Results:** Among patients with CAD in 36.6% of cases there is some form of GDZ lesion, while the proportion of patients with stable CAD accounts for 71.6% of cases, and 28.4% - for acute forms of CAD. The documented (visually confirmed on EGDS) presence of GDZ lesions was detected in 25.8% of cases, of which 67.5% were asymptomatic. At the same time, the presence of gastralgic symptoms (without a picture of EGDS lesion) was observed in 10.7% of cases among all patients with CAD. The acute form of CAD most often (34.4%) occurred among persons who had only gastralgic symptoms, without a picture of EGDS lesion, which should always remind doctors (therapists, cardiologists, gastroenterologists and surgeons) about atypical variants of the course of CAD. The latter in our study was 1.7% of cases. Among individuals with asymptomatic GDZ lesions, an acute form of CAD was observed in 28.8% of cases, and among patients with positive symptoms and EGDS-picture - in 20.0% of cases. The angiographic features of patients with CAD & with combined lesions of the GDZ turned out to be, comparatively, a lower incidence of complex (type "B" and "C") stenosis, according to the ACC / ANA classification (all $p > 0.05$). However, patients with asymptomatic GDZ lesions were characterized by a more frequent occurrence of lesions of the basins of the left coronary and anterior descending arteries, which once again emphasizes the mandatory nature of the EGDS study before performing interventional operations in patients with CAD. Among patients with gastralgic lesions ($n = 107$), a decrease in Hb level occurred in 27.1% of cases, of which 9.8% were associated with asymptomatic GDZ lesions. **Conclusion:** In order to timely diagnose and prevent dangerous complications of GDZ diseases, it is advisable for all patients with CAD to conduct an EGDS study.

Relevance

The general tendency towards an aging of the population and, as a consequence, an increase in the number of persons with comorbid conditions and diseases, among which diseases of the cardiovascular system (CVS) are more prevalent, contributes to an increase in the intake of various medications. Many patients with coronary artery disease (CAD) take low doses of acetylsalicylic acid (ASA) prescribed by cardiologists for the primary and secondary prevention of cerebrovascular and cardiovascular complications, or drugs that inhibit platelet aggregation (clopidogrel), recommended for a long time after stenting in coronary arteries (CA), which significantly increase the risk of adverse reactions from the gastrointestinal tract (GIT).

As evidenced by clinical experience, when taking non-steroidal anti-inflammatory drugs (NSAIDs), which include ASA, all parts of the GIT can be affected, but the most frequent and dangerous consequences is damage to the gastroduodenal zone (GDZ), primarily the antrum of the stomach - erosion, ulcers, bleeding and perforation.^[1,2]

The interaction between the GIT and the CVS is of undoubted interest. The characteristic clinical features of ischemic erosive and ulcerative lesions of GDZ are the absence of seasonality of exacerbations and anamnesis of the disease, atypical clinical picture, the presence of concomitant cardiovascular diseases (CVD), manifestation of the disease in the form of bleeding, etc.^[3] It was found, that most often ischemic erosive-

ulcerative lesions of GDZ occur in CAD in combination with dyslipidemia (DLP), while the main pathogenetic moment is considered atherosclerosis of the arteries, which accounts for 62-90% of cases of GDZ lesions.^[4-6] Nevertheless, the question of the relationship between GDZ lesions and coronary angiographic (CAG) characteristics in patients with CAD is controversial. In this regard, we conducted a pilot study, the purpose of which was: analysis of lesions of the gastroduodenal zone in relation to angiographic and clinical laboratory parameters in patients with coronary artery disease.

MATERIAL AND METHODS

In the period from 03/01/2021 to 09/01/2021, 298 patients with coronary artery disease were examined, who underwent CAG and percutaneous coronary intervention (PCI) with stenting. The average age of the respondents was 60.6 ± 9.3 years. The ratio of men and women was 199/98, i.e. 2/1.

Angiographic films were analyzed using appropriate software with the participation of at least two researchers. CAG was performed polypositionally, in 6 standard projections for the left coronary artery (LCA) and 3 projections for the right (RCA). CAG data were analyzed by determining the type of myocardial blood supply and localization of CA lesions by segments. The type of blood supply to the myocardium was determined by the source of blood supply to the inferior lateral wall of the LV. Stenoses up to 50% in diameter (less than 70% in area) were regarded as borderline, and more than 50% as pronounced (more than 70% in area). According to the CAG data, the following indicators were assessed: single and multi-vessel lesions; the average number of vascular lesions; the total number of stenotic segments (SS); the average number of SSs per patient; total number of implants; the average number of implants per patient; the average length of the atherosclerotic lesion (L, mm) and the average diameter of the affected artery (d, mm). The study also used the data processing method - SYNTAX-Score, which was carried out using an on-line calculator at the site <http://www.syntaxscore.com>.

To study the presence and severity of gastralgic symptoms in patients with CAD, we assessed the main and most frequent complaints associated with gastrointestinal lesions: belching, nausea, vomiting, heartburn and epigastric pain.

All patients, in addition to general clinical laboratory and functional research methods, underwent esophagogastroduodenoscopy (EGDS) in order to assess the localization and nature of the lesions. The gastroscopy was performed in a specially office with all the necessary equipment. EGDS was performed in the morning on an empty stomach. The patient received the last meal the day before, no later than 7 pm in the form of a light supper. The patient lay down on a couch in a horizontal position on his left side with knees bent to the chest. The oral cavity was treated with an antiseptic

(lidocaine) and then a special mouth guard was inserted. Further, after a deep breath, a gastroscope was introduced to the patient through the mouth. Also, a saliva ejector was inserted so that saliva does not interfere with the process. Next, a gastroenterologist, under visual control, conducted an endoscope into the esophagus, stomach and duodenum, while examining their inner surfaces. The enlarged image was displayed on the monitor. The duration of the procedure took about 15-20 minutes.

Statistical processing of the results was carried out on a Pentium-IV personal computer using the STATISTICA 6 software package. Calculated arithmetic mean (M), root mean square (standard) deviation (SD). To compare the arithmetic means of the two groups (control and experimental), we used Student's t-test. To assess the presence of links between the indicators, a correlation analysis was carried out with the calculation of the Pearson correlation coefficient. The χ^2 test was used to analyze the reliability of differences between qualitative characteristics. All values are presented as $M \pm SD$. Differences were considered significant at $p < 0.05$.

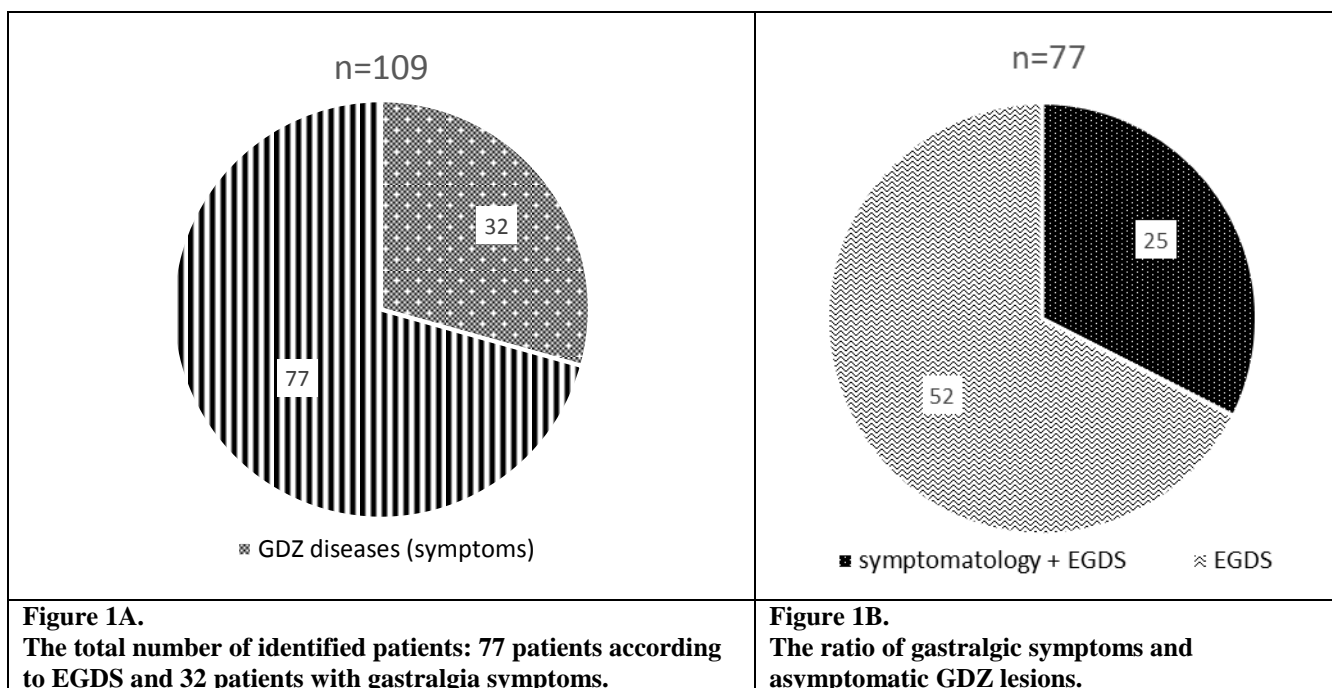
RESULTS

According to the analysis of complaints and conducted EGDS, 109 (36.6%) patients with one or another picture of gastralgic lesions were identified: in 77 respondents (25.8% of all 298 people), GDZ lesions were diagnosed based on the EGDS-data and 32 (10.7% of 298) had only gastralgic symptoms (i.e., there were complaints), and no GDZ lesions were detected on EGDS (Fig. 1A). The *Helicobacter pylori* (HP) test was positive in only 2 patients.

The analysis of complaints showed that out of the entire sample (298 patients), the presence of belching was noted by 6 (2.0%) patients, nausea - 10 (3.4%), vomiting - 15 (5.0%) and heartburn - 23 (7.7%) of the respondent. Complaints of pain in the epigastrium were noted by 9 (3.0%) patients, while in 4 of them the pain syndrome was justified by the presence of a lesion in the GDZ, and in 5 there was an atypical variant of angina pectoris, which accounted for 1.7% of the total the studied sample.

Analysis of the anamnestic data for medicinal products (MPs) taken, including ASA-containing ones, found that the average rate of medicinal products taken per day (\sum MP / day) in the group as a whole ($n = 298$) was 3.5 ± 2.0 units, while the share of ASA-containing was 69.1%. Directly in patients with a particular pattern of gastralgic lesions ($n = 109$), the \sum LP / day index was 3.7 ± 1.8 units, and the proportion of ASA-containing ones was 70.6%.

Of 77 patients with GDZ lesions identified during EGDS, 25 (32.5%) had one or another gastralgic symptomatology, in the remaining 52 (67.5%) cases of GDZ lesions were asymptomatic (Fig. 1B).



Evaluation of the nosological structure among 32 patients, who had only a gastralgic symptom, without EGDS signs of GDZ lesion, revealed that 11 (34.4% of 32) people had CAD with an acute course in the form of 5 cases of STEMI, 3 - NSTEMI & 3 - unstable angina pectoris. The remaining 21 (65.6% of 32) patients were diagnosed with CAD, stable angina FC III.

Among 52 patients who had asymptomatic GDZ lesions (i.e., the presence of EGDS signs of GDZ lesions), 15 respondents (28.8% of 52) had acute CAD (11 - STEMI, 1 - NSTEMI & 3 - unstable angina) and 37 (71.2% of 52) had stable angina FC III.

Out of 25 patients with complaints and EGDS-picture of GDZ lesion, acute CAD was observed in 5 (20.0% of 25) cases (2 - STEMI, 2 - NSTEMI & 1 - unstable angina), in the remaining 20 patients (80.0 % of 25) - stable angina FC III.

Those, out of 109 people with one or another picture of gastralgic lesions, 78 (71.6%) had stable CAD and 31 (28.4%) had an acute form of CAD.

A more detailed analysis of 77 patients (with EGDS signs of GDZ lesions) to assess the localization of the lesions established the following picture:

- the share of the stomach accounted for 81.8% (63 patients) of cases, while more often in the body area (30 b / x - 47.6%) and lesser curvature (21 b / x - 33.4%), less often - in fundal (7 b / x - 11.1%) and antrum (5 b / x - 7.9%) departments;
- localization in the duodenum (mainly in its bulb) was registered in 13.0% (10 patients) of cases;
- In the remaining 5.2% of cases (4 patients), a combined lesion of the stomach and duodenum was revealed.

In most cases (97.4%), the lesions were superficial (erythematous gastropathy, gastritis, bulbitis, etc.) or already healed lesions. Deep lesions, in the form of acute ulcers, were detected in 2 patients (0.7% or 1.8% of 109 patients with gastropathy), and therefore they were refused CAG until the state of the mucous membrane of the GDZ stabilized. Gastrointestinal bleeding (GIB) was not detected in any patient.

Analysis of CAG data was carried out in all 107 patients (2 patients, as mentioned above, dropped out of the study due to exacerbation of peptic ulcer disease). The control group included ischemic heart disease patients who had only gastralgic symptoms without the presence of EGDS-signs of GDZ lesion (n = 32); A-group consisted of 24 patients with complaints and EGDS-signs of GDZ lesion; The B-group consisted of 51 patients with asymptomatic, detected only during EGDS, damage to the GDZ. From these positions, it was found, that in patients of groups A and B, the mean score on the SYNTAX scale was higher (by 4.6 and 5.8 points, respectively), than in patients in the control group (Table 1).

In terms of the number of single- and multi-vessel lesions, the groups did not differ significantly (all $p > 0.05$), but among the patients of the B-group, multi-vessel lesions were encountered (by 6.9% and 5.8%) more often than in the A-group and control group. Nevertheless, such indicators as the average number of SS per patient and the average number of implants per patient in patients of groups A and B were less, than in patients in the control group (Table 1).

Analysis of the frequency of occurrence of lesions of the main coronary basins in the analyzed groups of patients established the following picture:

- lesions of the LCA-trunk were observed in the control group in 2 (6.2%) patients; in group A - in 2 (8.3%) and in group B - in 8 (15.7%) respondents;
- lesion of the right coronary artery (RCA) - in 19 (59.4%) people from the control group; 13 (54.2%) - from the A-group and 30 (58.8%) - from the B-group;
- lesion of the left anterior descending artery (LAD) - in 21 (65.6%) patients from the control group; 19 (79.2%) - from the A-group and 43 (84.3%) - from the B-group;
- lesions of the circumflex artery (CA) - in 13 (40.6%) individuals from the control group; in 13 (54.2%) - from the A-group and in 29 (56.9%) from the B-group.

Thus, among patients in the B-group (i.e., with asymptomatic lesions of the GDZ), lesions of the basins of the LCA-trunk (15.7%) and LAD (84.3%) were most often encountered. The groups did not differ significantly in the lesions of the remaining coronal basins.

Among other CAG-parameters, attention was drawn to the fact that the average length of atherosclerotic lesions (L) was the smallest in patients of the A-group.

The average postdilation pressure (P) in the control group was higher than in the A and B groups. This was probably due to the greater stiffness of the atherosclerotic plaque. Namely, the incidence of C-type stenosis (according to the ACC / ANA classification^[7]) among patients in the control group was higher than in groups A and B, by 4.8% and 7.0%, respectively (Table 1).

Table 1: Angiographic parameters of patients with coronary artery disease with GDZ lesions (n = 109).

Sign	Control group (Symptoms, without EGDFS-lesions of GDZ (n = 32))	A-group (EGDS-lesions with symptoms (n = 24))	p1	χ^2	B-group (EGDS-lesions without symptoms (n = 51))	p2	χ^2
Average SYNTAX score	17,2±9,9	21,8±9,6	0,087		23,0±9,1	0,008	
Single-vascular, n (%)	11 (34,4%)	8 (33,3%)	0,839	0,041	14 (27,5%)	0,672	0,179
Multi-vascular, n (%)	21 (65,6%)	16 (66,7%)			37 (72,5%)		
Average number of CA per 1 patient	2,19±1,17	2,16±1,34	0,929		2,54±1,43	0,249	
Total number of SS	54	32			67		
Average number of SS per 1 patient	1,69	1,33			1,31		
Total number of implants	46	28	0,982	0,001	62	0,316	1,006
Average number of implants per 1 patient	1,44	1,17			1,22		
Stenosis type "A"	18 (33,3% of 54 CC)	14 (43,7% of 32 CC)	0,462	0,541	29 (43,4% of 67 CC)	0,353	0,863
Stenosis type "B"	21 (38,9% of 54 CC)	10 (31,3% of 32 CC)	0,631	0,231	23 (34,3% of 67 CC)	0,743	0,108
Stenosis type "C"	11 (20,4% of 54 CC)	5 (15,6% of 32 CC)	0,795	0,068	9 (13,4% of 67 CC)	0,438	0,601
Mixed type	4 (7,4% of 54 CC)	3 (9,4% of 32 CC)	0,932	0,007	6 (8,9% of 67 CC)	0,980	0,001
Average L of defeat, mm	31,29±9,40	27,52±8,04			31,66±10,05		
Wed d KA, mm	3,18±1,46	3,06±0,46	0,700		2,96±0,35	0,305	
Average P, atm.	14,80±3,02	13,70±2,66	0,529		13,89±2,43	0,622	
Immediate angiographic success of the PCI procedure, n (%)	32 (100%)	24 (100%)			51 (100%)		

Notes: n - number of patients; CA - coronary arteries; SS - stenotic segment; L – is the length of the defeat; d – is the diameter of the artery; P - balloon inflation pressure during stenting; p1 - reliability of differences in the A-group in comparison with the control group and p2 - reliability of differences in the B-group in comparison with the control group.

This was confirmed by the analysis of laboratory parameters. In particular, the correlation analysis established an inverse relationship with the values of triglycerides (TG) in the blood ($p = 0.156$, $r = -0.298$, $t = -1.466$). Those, in patients of the control group, comparatively high levels of TG were recorded, than in individuals of groups A and B. Namely, the average blood TG values in the control group = 2.45 ± 1.52 mmol / l; in group A = 1.80 ± 0.58 mmol / l ($p = 0.052$ in comparison with the control group); in group B = 1.63 ± 0.74 mmol / l ($p = 0.001$ in comparison with the control group). With the values of total cholesterol (TC), there was a direct correlation dependence ($p = 0.259$, $r = 0.239$, $t = 1.158$), but not significant. The average values of the TC level in the groups were: 4.77 ± 1.94 mmol / l - in the control group; 5.50 ± 1.13 mmol / L - in the A-group ($p = 0.106$ in comparison with the control group) and 4.95 ± 0.86 mmol / L - in the B-group ($p = 0.564$ in comparison with the control group).

Since lesions of the GDZ mucosa are often accompanied by "latent" / minor bleeding, analysis of the level of hemoglobin in blood (Hb) was of interest. From these positions, it was revealed that of all patients with one or another gastralgic lesion ($n = 107$), the decrease in Hb took place only in 29 (27.1%) patients. At the same time, the reference values of the Hb level in these patients amounted to 113.86 ± 6.12 g / l. Of 29 patients with a low blood Hb content, 13 (44.8% or 40.6% of 32) were from the control group ($Hb = 114.46 \pm 4.43$ g / L), 11 (37, 9% or 45.8% of 24) - from the A-group ($Hb = 116.80 \pm 2.95$ g / l; $p = 0.150$) and 5 (17.2% or 9.8% of 32) - from the B-group ($Hb = 111.82 \pm 8.27$ g / l; $p = 0.357$). Nevertheless, when conducting a correlation analysis between GDZ lesions and the number of patients with an Hb level < 120 g / l, an inverse relationship was found that did not reach the level of reliability ($p = 0.099$, $r = -0.158$, $t = -1.659$).

The parameter $\sum LP$ / day for patients in the control group was 4.3 ± 1.9 units, while the proportion of ASA-containing drugs was 71.9%; in group A, similar data were 3.6 ± 1.9 units ($p = 0.178$) and 79.2% ($p = 0.755$; $\chi^2 = 0.097$) and in group B - 3.4 ± 1.8 units. ($p = 0.033$) and 66.7% ($p = 0.799$; $\chi^2 = 0.065$), respectively. Correlation analysis between the level of Hb blood and the presence of intake of ASA-containing drugs revealed an inverse relationship ($p = 0.156$, $r = -0.138$, $t = -1.426$), but not reliable. That is, in patients taking ASA-containing drugs, there was a tendency towards a decrease in the average blood Hb index.

DISCUSSION

The increase in the frequency of acute erosive and ulcerative gastroduodenal lesions (EUGL) in patients with CVD and other somatic pathology allows us to speak, in fact, of their epidemic. According to different authors, the frequency of EUGL in such patients reaches 80-90%, and that of the associated gastrointestinal tract infections - 45-55%. The widespread prevalence of

EUGL is associated with the aging of the population, the influence of unfavorable ecology, exogenous (alcohol, etc.) and endogenous intoxications, iatrogenic factors (an increase in the number and volume of surgical interventions, taking various drugs).^[8-13] In our study, the proportion of detected GDZ lesions was 36.6%, of which the exacerbation of ulcers was in 2 (1.8%) patients. All patients still took various drugs at the outpatient stage, while the proportion of ASA-containing ones was 69.1%, and among those with gastralgic symptoms - 70.6%.

In the study "SUMMARY" AstraZeneca, in patients with coronary artery disease, erosive and ulcerative lesions were localized mainly in the stomach (88%), lesions in the duodenum were observed in 8% of patients, and combined lesions of the stomach and duodenum were found in 4% observations.^[11,15] Our results turned out to be consonant with these data. Namely, in our study, gastric lesions were observed in 81.8% of the examined, localization in the duodenum was recorded in 13.0% and combined lesions were observed in 5.2% of cases.

The urgency of the problem of erosive and ulcerative lesions of the stomach and duodenum associated with the use of NSAIDs (the so-called NSAID-associated gastropathy) is primarily due to the fact that the use of drugs in this group is extremely common among the population. In Great Britain, for example, more than 24 million prescriptions of drugs of this group are registered annually.^[16] About 70% of people over 65 in the United States take NSAIDs at least once a week, 34% - daily.^[17] The volume of annual sales of these drugs in the United States reaches 6 billion dollars.^[18] In our study, 69.1% of patients noted the intake of ASA-containing drugs, while among those with an asymptomatic form of GDZ lesion this indicator was 66.7%. However, it should be borne in mind that taking ASA-containing drugs is mandatory as part of double antiplatelet therapy in patients with CAD who underwent PCI with stenting and as monotherapy for the prevention of CAD. Representative studies have established that the use of ASA and NSAIDs in 1/3 of patients with a high risk of coronary artery occlusion causes a statistically significant decrease in the risk of myocardial infarction and stroke, as well as deaths.^[19-20] Nevertheless, despite the high efficiency, the use of ASA in 25% of cases is accompanied by the development of side effects, the most significant of which are NSAIDs – gastropathy.^[20,21]

In our study, according to CAG data, patients with GDZ lesions were characterized by a lesser incidence of complex types of SS, but their frequent localization in the basins LCA-trunk and LAD in individuals with an asymptomatic course of gastropathies.

According to the literature, consideration of the problem of the comorbidity of ischemic heart disease and stomach diseases from the local positions of the interaction of several specific pathologies is not always able to identify the general pathogenetic mechanisms of this condition.

According to some authors, the study of general risk factors, the current imbalance in the work of the sympathetic and parasympathetic nervous systems, the specifics of dyslipidemic processes still does not allow considering the combination of CAD and GIT-pathology as a fully integrated process. At the present stage, there are a number of publications in favor of considering the state of the combined course of CAD with GIT-pathology from general positions based on endothelial dysfunction.^[22,23] Endothelial dysfunction is the primary process for the local development of atherosclerotic lesions in the vessel wall. An early trigger of atherogenesis is damage to the endothelium by various factors affecting the lumen of the artery. Lipid metabolism disorders are a risk factor, the correction of which underlies the prevention of CVD. The very concept of "lipid metabolism disorder" or DLP includes a wide range of lipid metabolism disorders. Currently, the main importance for assessing the prognosis and efficacy of DLP treatment is given to the levels of TC and low-density lipoprotein cholesterol (LDL-C). Among other disorders of lipid metabolism, the important role of elevated TG levels in the development of atherosclerosis should be noted.^[24,27] The results of our study established an inverse correlation between the values of TG and gastropathy and a direct relationship with the level of TC, which can be considered as an indirect confirmation of the commonality of the positions of the underlying endothelial dysfunction and GDD lesions.

Diseases of the GIT rank first in the structure of causes of iron-deficiency anemia in men and women in postmenopausal women and second in women before menopause. At the same time, GIT-pathology can be the cause of other types of anemia (B12-deficiency, folic acid deficiency, etc.).^[28,29] However, in our work, a decrease in the blood Hb level took place only in 27.1% of cases, while the correlation between the groups of patients and the presence of a low blood Hb level was inverse, which did not reach the level of reliability.

CONCLUSION

Among patients with CAD in 36.6% of cases there is some form of GDZ lesion, while the proportion of patients with stable CAD accounts for 71.6% of cases, and 28.4% - for acute forms of CAD.

The documented (visually confirmed on EGDS) presence of GDZ lesions was detected in 25.8% of cases, of which 67.5% were asymptomatic. At the same time, the presence of gastralgic symptoms (without a picture of EGDS lesion) was observed in 10.7% of cases among all patients with CAD.

The acute form of CAD most often (34.4%) occurred among persons who had only gastralgic symptoms, without a picture of EGDS lesion, which should always remind doctors (therapists, cardiologists, gastroenterologists and surgeons) about atypical variants

of the course of CAD. The latter in our study was 1.7% of cases. Among individuals with asymptomatic GDZ lesions, an acute form of CAD was observed in 28.8% of cases, and among patients with positive symptoms and EGDS-picture - in 20.0% of cases.

The angiographic features of patients with CAD & with combined lesions of the GDZ turned out to be, comparatively, a lower incidence of complex (type "B" and "C") stenosis, according to the ACC / ANA classification (all $p > 0.05$). However, patients with asymptomatic GDZ lesions were characterized by a more frequent occurrence of lesions of the basins of the left coronary and anterior descending arteries, which once again emphasizes the mandatory nature of the EGDS study before performing interventional operations in patients with CAD.

Among patients with gastralgic lesions ($n = 107$), a decrease in Hb level occurred in 27.1% of cases, of which 9.8% were associated with asymptomatic GDZ lesions.

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