



MODERN TREATMENT OF GASTRIC CANCER RELEVANCE OF THE PROBLEM

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Article history:	Abstract:
Received: 20 th June 2024 Accepted: 14 th July 2024	Cancer is a malignant tumour that has autonomous and progressive growth. In foreign medical literature, the term is often used to refer to all malignant tumours, regardless of their origin or tissue composition. Each tumour may have its own characteristics and propensity to form metastases, so a cancerous tumour behaves differently in the body [1]. Gastric cancer is the third leading cause of cancer-related mortality worldwide. More than 95% of gastric cancers are adenocarcinomas, which are usually classified based on anatomical localisation and histological type. Gastric cancer usually has a poor prognosis as it is often diagnosed at an advanced stage [2]. Any cell in the body can become malignant. And the treatment methods that can fight cancer will depend on its characteristics. Cells of almost all our organs are different from each other, moreover, cells of one organ can also be different. Therefore, speaking about stomach cancer, it should be noted that this is a group of diseases that are caused by different reasons, proceed in different ways and require different treatment approach [12].

Keywords: initial gastric cancer, classification, definition, carcinoma in situ, severe dysplasia, intraepithelial neoplasia.

RELEVANCE : Relevance of the study. Gastric cancer (GC) is a malignant epithelial tumour that develops from the gastric mucosa. According to the International Agency for Research on Cancer, RG ranks 4th in prevalence and 2nd in the world in the structure of cancer mortality. According to world statistics, the highest prevalence of this pathology is noted in Asian countries such as Japan, Korea and China, as well as in South and Central America and Western Europe. Men get the disease about 2 times more often than women. The number of patients increases significantly at the age of over 50 years old [3].

Gastric cancer is most common in Japan, Finland, Chile, Iceland, and several times less common in the USA, Mexico, and Equatorial Africa. The maximum level of gastric cancer incidence was observed in Japanese men (114.70 per 100,000 population), the minimum - in white women in the USA (1.30 per 100,000 population). The highest rates are also registered in China, Belarus, Russia, Estonia, Latvia and New Zealand. Relatively low incidence (3.70-4.90 per 100,000 population) is observed in Sweden, Switzerland, USA, Canada, France. In the USA for the last 40 years annual mortality from gastric cancer has decreased from 30 to 8 people per 100 thousand population. A less marked decrease in mortality has been noted in Western and Eastern

European countries. Over the last 50 years, the incidence and mortality from gastric cancer have decreased worldwide, especially in economically developed countries. This process is attributed to improved socio-economic conditions and increased consumption of fresh fruit and vegetables and vitamins. Studies investigating the causes of gastric cancer suggest the role of genetic predisposition, infectious agent and diet. Environmental exposure is an important factor influencing the incidence of the disease. When populations migrate from a high incidence area to a low incidence area, the incidence of cancer decreases, for example, in emigrants from Japan and China living in the United States, especially in the second and third generations. The most significant exogenous risk factor for the development of gastric cancer is a diet including meat, smoked meat, fat, high salt content. In contrast, consumption of fresh fruit, fibre, vitamins (especially beta-carotene, vitamin C) is protective. N-nitrosamines, especially endogenous N-nitrosamines, are one of the reliable causes of cancer development. The trigger is a decrease in the acidity of gastric juice, found in chronic gastritis, which promotes the development of pathogenic flora and an increase in the synthesis of nitroso compounds in the lumen of the organ. Food additives, especially nitrates used as preservatives, are



carcinogenic. Nitrates are also found in vegetables grown with excessive mineral fertilisers. Nitrates themselves do not cause cancer, but become carcinogenic when converted into nitrites by nitrate-reducing bacterial flora that appear in the stomach at intragastric pH 5.0 or higher. At the same time, foods rich in ascorbic acid may play a role as an inhibitor of carcinogenesis. In recent years, an association between *Helicobacter pylori* and the development of gastric cancer has been considered reliable. The mechanism of carcinogenesis associated with *Helicobacter pylori* is related to the ability of the microorganism to cause marked infiltrative gastritis with interstitial cell proliferation. *Helicobacter pylori* with the help of the enzyme extracellular urease breaks down urea with the formation of ammonia, activates the processes of lipid peroxidation, increases the concentration of free radicals, which stimulates the processes of carcinogenesis and increases the risk of cancer by 3.8 times [4].

The standard scope of surgery in the treatment of early cancer is similar to the more common forms and includes subtotal gastric resection or gastrectomy with lymphadenectomy. Taking into account the low frequency of second-order lymph node involvement, according to the recommendations of the Japanese Association for Gastric Cancer CR574 19 (A), an adequate and sufficient volume of lymphadenectomy for T1 tumours is the removal of perigastric lymph nodes, as well as lymph nodes #7; 8a; 9 (lymphadenectomy D1 [5].

MATERIALS AND METHODS : The material of the study was literature data presented in scientific articles, textbooks, journals.

RESULTS: To date, there is no clearly justified adjunctive treatment for RR. Careful preoperative investigation is aimed at establishing or morphological confirmation of the diagnosis and formulating a treatment plan. As additional modalities are ineffective, surgical intervention is the only chance for cure [13]. There are a number of patterns of metastasis of rectal cancer depending on the region in which the tumour is located. Upper ampullary cancer most often metastasises to lymph nodes along the a. rectalis superior, a. mesenterica inferior and aorta (ascending pathway). rectalis superior, a. mesenterica inferior and aorta (ascending route of metastasis), lower and mid-ampullary cancers - to iliac lymph nodes, middle rectal and zaryngeal lymph nodes (lateral route of metastasis), in anal cancers - to inguinal lymph nodes (descending route of metastasis). T. Takahashi et al. (1997). [14]. For a long time, 5-fluorouracil and its derivatives remained the only drugs active in this form

of malignant tumours. In the 90s of the 20th century, fundamentally new drugs with antitumour activity in colorectal cancer entered oncological practice: irinotecan, platinum derivative of III generation oxaliplatin, raltitrexide, as well as new oral fluoropyrimidines - UFT and capecitabine. Clinical studies of these drugs have shown that their use in drug combinations can improve the overall efficacy of chemotherapy in patients with colorectal cancer and increase their chances of prolonging life. Studies have shown that the median survival rate of patients with metastatic colorectal cancer with purely symptomatic therapy was only 8 months, with chemotherapy using a combination of 5-fluorouracil and leucovorin increased to 12 months, with the use of modern chemotherapy with combinations including irinotecan and oxaliplatin increased to 15-17 months, and with the sequential use of these combinations containing irinotecan or oxaliplatin increased to 20 months [15]. Regional lymph node involvement in gastric cancer is one of the leading prognostic factors. The overall incidence of lymphogenic metastasis in gastric cancer reaches 47.7% and directly depends on the depth of invasion. In T1 tumours the frequency of lymph node involvement does not exceed 10-15%, while in T4b tumours it reaches 90%. The most frequently affected lymph nodes in gastric cancer are lymph nodes of the 1st and 2nd order (nos. 1-11) - 15.7 and 20.3%, respectively (IB). The standard scope of intervention on the lymphatic system in gastric cancer is currently considered to be the removal of lymph nodes of the 1st and 2nd order (extended lymphodissection D2). Routine performance of paraaortic lymphadenectomy (D3) is inappropriate (A), as it does not improve patient survival and is accompanied by a higher incidence of complications (IA) In randomised trials it has been shown that administration of oral fluoropyrimidine S1 for 12 months after surgical treatment with D2-lymphodissection. in stage II-III gastric cancer resulted in a significant improvement in 3-year RR from 70.1% to 80.1%, and administration of a postoperative XELOX regimen for 6 months (Ib) resulted in an increase in 3-year RR from 59% to 74%. Possible in pT2-4N1-3 (1b, A) tumours. 3 courses of polychemotherapy with CF, ECF, ECX or EOX regimens are performed, then, if there are no signs of non-resectability, surgery is performed, after which 3 more cycles of similar chemotherapy are administered (6 cycles in total). The efficacy of perioperative chemotherapy in patients with gastric cancer was first shown in the MAGIC study (n=503), which also included patients with resectable cardioesophageal cancer and oesophageal adenocarcinoma. CR574 20 combination treatment improved not only the 5-year BRV but also



the OS (18) (1b). In a similar French study, perioperative chemotherapy with a CF programme resulted in a significant increase in 5-year survival: recurrence-free survival from 19% to 34% and overall survival from 24% to 38% ($p=0.02$) (19) (1b). The results of these studies suggest that perioperative chemotherapy may be an alternative to postoperative chemoradiotherapy for operable gastric cancer in D0-1 lymphodissection. The expediency of additional to surgical treatment in D2 lymphodissection remains controversial. Currently, perioperative chemotherapy is included in the standard of care for operable gastric cancer patients in many European countries (A), while the administration of adjuvant chemotherapy to patients who did not receive chemotherapy at the preoperative stage is not standardised [6].

It is currently assumed that classifications of RR based on the features of genotypes and molecular phenotypes of this malignant disease may prove to be more prognostically effective than traditional histopathological classifications. They will allow a precise approach to the choice of therapeutic tactics and expand the possibilities of using targeted or immunotherapy. The search for 'hot spots' of oncogenesis signalling pathways is currently a priority task. Identification of HER2-positive special molecular-genetic with important therapeutic significance is the result of more than 30 years of fundamental and clinical research of the most important signalling pathways responsible for the implementation of stimuli of cell growth and proliferation through the family of tyrosine kinase receptors. This subgroup has found its place in modern molecular genetic classifications of RR, such as the Singapore-Duke study [7, 8] and the TCGA (The Cancer Genome Atlas Programme) [9-10] [9-10]. As a result of these studies, the detection rate of RRH increased from 15.2% (2011) to 24.7% (2019) or 1.6-fold. In group 1, 30 patients (11.3%) underwent surgical treatment in the volume of abdominal gastrectomy with lymphodissection in the volume of D-1, 72 patients (27.1%) underwent subtotal distal gastric resection according to Bilioth-II with lymphodissection in the volume of D-1. The average age was 66.1 ± 10.5 years. The indications for these surgical interventions were inconsistency of the patient's examination data with the absolute indications for intraluminal surgery: differentiated adenocarcinoma up to 2 cm in size. Endoscopic examination with the use of additional imaging techniques, such as chromogastrosocopy and magnifying narrow-spectral gastroscopy, revealed 8 (7.8%) neoplasms of 0-Ip type, 0-Is - 2 (1.9%), 0-IIa - 6 (5.9%), 0-IIc - 4 (3.9%), 0-IIa+IIc - 38 (37.3%), type 0-III - 44 (43.2%). In 36 cases (35.3%) endoscopic

examination revealed tumour ulceration. The location of the tumour process on the posterior wall of the antral and greater curvature of the stomach was noted with equal frequency and these localisations prevailed - 22 cases (21.6%) each. With less frequency, in 21 (20.6%) and in 20 (19.6%) cases the tumour was located on the greater curvature and lesser curvature in the middle third of the stomach body, respectively. The size of the mucosal tumour lesion averaged 27.8 ± 12.9 cm. Morphologically moderately differentiated adenocarcinoma prevailed in 34 (33.4%) cases, in other observations adenocarcinoma of high and low degree of differentiation was revealed in 26 (25.5%) and 24 (23.5%), respectively. Undifferentiated adenocarcinoma was registered in 18 cases (17.6%). Lymphovascular invasion in the tumour micro specimen was diagnosed in 4 cases (3.9%). The pathological stage of the tumour process was determined as T1aN0M0 in 28 (27.5%) cases, T1bN0M0 - in 74 (72.5%) cases [11].

Conclusion: It is recommended that in the first 1-2 years physical examination and collection of complaints should be done every 3-6 months, in 3-5 years - once every 6-12 months. After 5 years from the date of surgery, visits are performed annually or when complaints arise. In patients with a high risk of recurrence, the interval between examinations can be shortened.

As a result of the study, a significant proportion of patients had precancerous diseases, which proves the importance of these pathologies in the development of gastric cancer. The more frequent precancerous disease was considered to be a permanent gastric ulcer, and the more widespread risk factor was smoking. Thus, the importance of the primary care physician lies in the manifestation of 'oncological vigilance', timely diagnosis, treatment and observation due to patients with precancerous diseases, as well as reducing the impact of risk factors in the human body.

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