



Наукові перспективи
Видавнича група

Перспективи та інновації науки



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Журнал заснований з метою розвитку наукового потенціалу та реалізації кращих традицій науки в Україні, за кордоном. Журнал висвітлює історію, теорію, механізми формування та функціонування, а, також, інноваційні питання розвитку медицини, психології, педагогіки та. Видання розраховано на науковців, викладачів, педагогів-практиків, представників органів державної влади та місцевого самоврядування, здобувачів вищої освіти, громадсько-політичних діячів.

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RISK FACTORS OF THE OCCURRENCE OF GASTRIC MALIGNANT NEOPLASMS - POSSIBLE ORGANIZATIONAL FORMS AND MODELS OF THEIR PREVENTION

Abstract. The problem of malignant neoplasms of the stomach in Ukraine should be considered as an important medical and socio-economic phenomenon, the acuteness and relevance of which are increasing significantly due to the unfavorable

demographic situation (pronounced aging of the population) against the background of adverse environmental conditions, including the negative impact of the consequences of the accident at the Chernobyl nuclear power plant, as well as the unstable socio-economic and political situation, which became incredibly aggravated during the COVID-19 pandemic (as in other countries of the world), as well as in the conditions of military aggression of the Russian Federation. Accordingly, in the current socio-economic and political conditions of Ukraine, it is not possible to build any strategies to combat malignant neoplasms (MN) without taking into account the generally low level of material income and awareness of the population, as well as chronic psycho-emotional stress, exacerbated by the COVID-19 pandemic and the war with the Russian Federation. As you know, it is an axiom that in order to prevent diseases, it is necessary to know both the etiological causes of their occurrence and the risk factors contributing to this.

Most risk factors for gastric malignancy (MNG) are manageable and therefore preventable. Accordingly, the prevention of cancer in general and MNGs in particular, according to WHO recommendations, should become a priority area of any health care system. At the same time, it is emphasized that the consequences of oncopathology depend not only on the presence of risk factors, but also on the population's awareness of them, early detection, timely and proper treatment and rehabilitation, that is, on medical and organizational factors.

In turn, the population's awareness of risk factors and access to medical care depend on social status, income level, and education level, which makes socioeconomic factors important general factors of chronic non-infectious diseases, including MNGs. Unfortunately, despite the seemingly wide awareness of the population with the help of the mass media and the efforts of health care institutions, the availability of various sources of information on the Internet, the level of awareness of citizens about early signs and methods of prevention of malignant neoplasms remains unsatisfactory.

Keywords: gastric cancer, prevention, risk factors, organizational models of prevention

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ЧИННИКИ РИЗИКУ ВИНИКНЕННЯ ЗЛОЯКІСНИХ НОВОУТВОРЕНЬ ШЛУНКУ - МОЖЛИВІ ОРГАНІЗАЦІЙНІ ФОРМИ Й МОДЕЛІ ЇХ ПРОФІЛАКТИКИ

Анотація. Проблему злоякісних новоутворень шлунку в Україні слід розцінювати як важливе медичне і соціально-економічне явище, гострота й актуальність якого значно зростають у зв'язку з несприятливою демографічною ситуацією (вираженням постарінням населення) на тлі несприятливих екологічних умов, у т.ч. негативного впливу наслідків аварії на Чорнобильській АЕС, а також нестабільної соціально-економічної і політичної ситуації, які наймовірно загострилися під час пандемії COVID-19 (як і в інших країнах світу), а також в умовах військової агресії російської федерації. Відповідно, в сучасних соціально-економічних та політичних умовах України не можливо будувати будь-які стратегії боротьби із злоякісними новоутвореннями (ЗН), не беручи до уваги загально низький рівень матеріальних доходів та поінформованості населення, а також хронічний психоемоційний стрес, посилений пандемією COVID-19 і війною з російською федерацією. Як відомо - аксіомою є те, що для запобігання хворобам, потрібно знати як етіологічні причини їх виникнення, так і чинники ризику, що сприяють цьому.

Більшість чинників ризику злоякісних новоутворень шлунку (ЗНШ) є керованими, а отже їм можна запобігти. Відповідно профілактика онкозахворювань загалом і ЗНШ зокрема за рекомендаціями ВООЗ повинна стати пріоритетним напрямом будь-якої системи охорони здоров'я. При цьому наголошується, що наслідки онкопатології залежать не тільки від наявності чинників ризику, а й від обізнаності населення щодо них, раннього виявлення, вчасного і належного лікування та реабілітації, тобто від медико-організаційних чинників.

У свою чергу, обізнаність населення про чинники ризику та доступ до медичної допомоги залежать від соціального статусу, рівня доходів та рівня

освіти, що робить соціально-економічні чинники важливими загальними чинниками хронічних неінфекційних захворювань, у т. ч. ЗНШ. На жаль, не дивлячись на здавалося б широку інформованість населення за допомогою засобів масової інформації (ЗМІ) та силами закладів охорони здоров'я (ЗОЗ), на доступність різноманітних джерел інформації в Інтернеті, рівень обізнаності громадян про ранні ознаки та способи профілактики злоякісних новоутворень залишаються незадовільними.

Ключові слова: рак шлунка, профілактика, чинники ризику, організаційні моделі профілактики

Formulation of the problem. Oncological diseases throughout history caused a desire to understand the cause of their occurrence and the very essence of diseases that brought death [1]. Depending on the degree of development of science, the characteristics of tumors were different [2]. In the last decade, the oncological situation in the world remains unfavorable in terms of the incidence and prevalence of cancer in both economically developed and developing countries [3]. At the same time, when analyzing the main trends in the treatment of patients with an oncological profile, it becomes obvious that in a number of countries of Western Europe and North America, health care systems managed to first stabilize and then reduce mortality from the most common malignant tumors. This is primarily due to the full-scale implementation of national screening programs [4]. Today, screening in oncology is almost the only method, the use of which helps to reduce the mortality rate from certain types of malignant neoplasms. Until now, the expediency of population screening of malignant neoplasms in Ukraine remains a subject of debate due to the lack of awareness of the population and doctors, the lack of a clear understanding of the concept and process of screening [5], the laboriousness and relatively high cost of screening methods of examination, insufficiently convincing evidence of the need to conduct it in relation to some nosology's malignant tumors.

Analysis of recent research and publications. Scientists include *Helicobacter pylori* (*H. pylori*) and Epstein-Barr virus (EBV) infection as possible etiological factors of CKD [6-8]. The role of *H. pylori* in the etiology of MNG has been confirmed by numerous experimental, epidemiological and prospective studies. It is clear that when looking for other significant risk factors for gastrointestinal tract diseases, a significant part of scientific research was concerned with the study of eating habits [9-11]. Scientists believe that it was the changes in the methods of food storage and cooking that took place in the middle of the 20th century, associated with the appearance of household refrigerators and the reduction of the use of salt as a natural preservative, that served as the first impetus for a further decrease in the incidence of MNG [11, 12]. The important role of genetic factors in the development of MN is also known [13-15]. In particular, scientists consider three genetic syndromes to be hereditary forms of MNG:

1) Hereditary gastric cancer of the intestinal type (HGCIT), caused by mutations of the CDH1 gene, which is responsible for the expression of the protein of intercellular contacts E-cadherin;

2) GAPPS syndrome (gastric adenocarcinoma & proximal polyposis of the gastric);

3) syndrome of familial gastric cancer of the intestinal type (FIGC).

Therefore, in order to reduce the incidence of gastric cancer and reduce the number of transformations of precancerous diseases into cancer, including gastric cancer, it is necessary to take preventive measures in a timely manner. Cancer prevention is understood as a complex of state, public and medical measures, which includes primary (preclinical), secondary (clinical), as well as tertiary (anti-recurrence) prevention of cancer [16-18].

Primary cancer prevention (PCP) is a system of state-regulated social and hygienic measures and efforts of the population itself, aimed at preventing the occurrence of cancer and precancerous conditions preceding them by eliminating, weakening or neutralizing the influence of adverse environmental and lifestyle factors, as well as by increasing non-specific resistance organism [18,19].

Mass examination of people who do not consider themselves sick to detect diseases at the earliest possible stage or other conditions (risk factors for future diseases) is called Screening. Wilson JMG and Jungner G in the work "Principles and practice of screening for disease detection", which was published in 1968 as a monograph of the World Health Organization (WHO) [20], first defined the main criteria of screening programs. These criteria remain relevant to this day, however, taking into account the stricter requirements of evidence-based medicine, the need to increase the effectiveness of screening programs, as well as to minimize side effects, they have been modernized and supplemented.

Modern criteria for evaluating the effectiveness, expediency and profitability of screening programs were developed by the National Screening Committee of Great Britain in 2015 [21]. These criteria must be taken into account when planning screening programs. At the same time, scientists emphasize that the form of cancer expected for screening must be an important health care problem for the country or region in which screening is carried out, that is, morbidity and mortality must be high.

The aim of the study to investigate the influence of risk factors on the development of malignant neoplasms of the stomach and to assess the state of the organization of prevention and the provision of medical care to patients.

Presenting main material. MNG is a polyetiological disease that occurs under the simultaneous influence and interaction of many risk factors, and an infectious agent can be only one of them.

According to the WHO, *H. pylori* infection belongs to group 1 carcinogens. The peculiarity of this microorganism is the ability to damage the gastric mucosa by releasing enzymes and toxins and thereby increase the vulnerability of the gastric

mucosa to acid-peptic damage. In addition, the body's immune response to *H. pylori* causes an inflammatory reaction, which in turn increases tissue. Chronic *H. pylori* infection and the atrophic gastritis caused by it significantly increase the risk of developing both types of MNG, and eradication therapy reduces this risk. However, the occurrence of a tumor in the gastric cannot be explained by the influence of only an infectious factor. After all, it has been established that *H. pylori* develops in a very small percentage of people infected with *H. pylori*. Incidence by region also does not coincide with infection (the highest infection in Africa, where the incidence of MNGs is low).

Food factors that reliably increase the risk of developing MNG are: consumption of excessive amounts of table salt, a diet with a high (more than 30 g/day) content of meat products prepared with the use of salt, smoking, preservatives (processed meat), as well as food nitrates and nitrate-containing components. It has been established that the consumption of table salt in large quantities leads to damage to the mucous membrane of the stomach, while its susceptibility to the influence of other carcinogenic factors increases. Excessive consumption of salty food is also associated with an increase in *H. pylori* infection, and their synergistic interaction causes the acceleration of processes leading to malignant transformation of the gastric mucosa.

Carcinogenic factors are also food nitrates and nitrate-containing compounds that enter the human body with the consumption of food, alcohol, tobacco smoke, and from other environmental sources. N-nitro compounds are formed after the consumption of nitrates, which are natural components of food products such as vegetables and potatoes, and are also used as food additives in the manufacture of some cheeses and sausage products.

The risk of MNG increases when unhealthy eating habits are combined with alcohol abuse, excess body weight ($BMI > 25$) and tobacco smoking, including smokeless.

Along with food, alcohol, and tobacco smoke, carcinogens from the natural environment: air, water, and soil also usually enter the human body.

Evaluating the hereditary factor, the most severe of the genetic syndromes is HGCIT, in which the lifetime probability of developing MNG exceeds 80%. This form of hereditary cancer is characterized by an early manifestation, an aggressive course and an extremely unfavorable prognosis. The average age of patients in whom a tumor occurs during HGCIT is only 38 years. One of the most likely genetic bases of this syndrome is a mutation of the *CDH1* gene, which is inherited in an autosomal dominant pattern.

The interrelationship between the occurrence of MN against the background of severe stressful situations, anxiety, and depression is clearly visible.

The risk of developing MNG can also increase as a result of some medical interventions. One of the main iatrogenic factors is a history of gastric resection. At the same time, malignant transformation after resection of the stomach according to

Billroth II is observed more often than after resection according to Billroth I. This may be related to the reflux of bile and pancreatic juice, which change the pH in the stomach and contribute to the maintenance of chronic inflammation of the mucous membrane. The risk of the development of MNG increases with an increase in the time that has passed since the surgical intervention.

Iatrogenic factors for the development of MNG include prolonged (for several years) use of proton pump inhibitors and H₂-blockers, as well as radiation exposure to the abdominal cavity due to Hodgkin's lymphoma, especially in combination with procarbazine.

On the other hand, the risk of developing cancer of the gastrointestinal tract, including that associated with *H. pylori* infection, can be reduced against the background of regular use of nonsteroidal anti-inflammatory drugs.

The strategic goal of primary cancer prevention (PCP) is to reduce the incidence of cancer in the population. The main directions of PCP were formed mainly during the last three decades and today it includes: oncohygienic prevention, biochemical (chemoprophylaxis), medical-genetic, immunobiological and endocrine-age prevention.

It has been practically proven that by following a certain diet you can significantly reduce the adverse (oncological) effects of food. In particular, you should avoid overeating, canned, pickled and smoked products and eat more fresh vegetables (including onions and, especially, garlic), vitamins (A, C), greens, fruits and natural juices, coarsely ground cereals, bread with bran, milk and dairy products. It is also necessary to give up smoking and strong alcoholic beverages (especially in combination with fatty, fried, smoked and salty food), control body weight and actively engage in physical work and sports.

In terms of correcting bad habits and lifestyle, great importance is currently attached to the consultations of medical professionals - doctors and/or nurses, mainly primary medical care (PMC). Numerous scientific studies have proven that clarification and advice on lifestyle changes received from a health professional is a more effective method in influencing some clinically significant outcomes and quality of life than receiving the same information from other sources. This applies to consultations on physical activity, diet, smoking cessation, weight correction, etc.

That is, ideally, PCP should be carried out in practically healthy people, but it is especially necessary for persons with a high risk of developing malignant neoplasms of the gastrointestinal tract, who have several risk factors or precancerous diseases. In particular, according to the recommendations of the United States Preventive Services Taskforce (USPSTF), adults >18 years of age with overweight, obesity, and other risk factors should be offered intensive (>360 min.) behavioral counseling on healthy eating and physical activity activities for the prevention of chronic non-infectious diseases and their complications. It is recommended to pay special attention to the prevention of stomach cancer in old age.

Patients infected with *H. pylori* are recommended to be prescribed anti-*Helicobacter* therapy.

Optimism and the ability to cope with negative emotional states play a very important role in the prevention of tumors. Some people need professional help in this matter in the form of a psychotherapist or psychologist consultation.

The strategic goal of secondary cancer prevention (SCP) is to detect the pathology as early as possible. After all, with timely detection, modern methods of treatment allow to significantly extend the patient's life, and in some cases, to defeat the disease. Successes in the development of methods of diagnosis and treatment of early forms of the disease have made it possible to distinguish the so-called "early MNG" (T1N0M0) as a practically curable disease. Radical surgical treatment at this stage ensures 10-year survival of 80-95% of patients. In this regard, regular medical examinations and diagnostic studies play an important role, the implementation of which depends both on the responsibility of the citizens themselves for their own health, and on the actions of medical professionals, primarily PMC.

MNG does not belong to the visual forms of cancer, and therefore, as was shown in section 1.1, it is often detected in the late stages. Therefore, an important task of secondary cancer prevention is the formation of cancer awareness among medical workers and the population (especially from risk groups), which includes an algorithm of actions aimed at the earliest possible detection of cancer, including stomach, with the slightest, even indirect, suspicion of them - with the use of the most effective methods of objective research. After all, orientation in diagnostics only to the clinical manifestations of MNGh (according to the principle of appeals) inevitably leads to the fact that only neglected forms of the disease are detected. This is fully applicable to the situation in Ukraine, where 82-84% of patients with MNG are still detected in stages T3-T4, while in Japan more than 64% of cases of the disease are diagnosed in stages T1-T2, which is associated with a well-established by the appropriate screening program.

In particular, with regard to the detection of MNG, its diagnosis today consists in detecting the tumor (primary diagnosis) and establishing the spread of the tumor process (secondary diagnosis or staging), both in the preoperative period and intraoperatively. Moreover, modern methods make it possible to detect the disease at sufficiently early stages, when the tumor is localized in the gastric mucosa and practically does not metastasize.

The main instrumental methods that allow you to detect MNG and confirm the diagnosis are: X-ray examination of the upper parts of the gastrointestinal tract and esophagogastroduodenoscopy. MNG can also be recognized during targeted ultrasound examination of the organ.

Among the newest methods designed to improve the diagnosis of stomach cancer and establish its prevalence, it should be noted multispiral computed tomography (CT) in the mode of 3-D reconstruction, and the so-called virtual endoscopy. Scientific data show that a three-dimensional image is more informative

in the recognition of early gastric cancer compared to an axial image. However, the diagnostic capabilities of this method are limited, as it is not possible to obtain morphological confirmation, assess the perigastric spread of the tumor (the need for repeated CT in the usual mode) and detect distant metastases. Therefore, the indications for the use of this method require further clarification.

Therefore, fibrogastroscopy with polybiopsy (from at least 5 places of the suspicious mucosal area) is considered the most accurate method of diagnosing MNG today, which should be performed by all patients with suspicion of MNG, except for those extremely rare cases when there are contraindications to the study. The most promising method of increasing the resolution of gastroscopy is laser fluorescence spectroscopy. This method is based on the ability of tissues to fluoresce when they are illuminated by a laser beam of a certain wavelength. Fundamentally important is the provision of active diagnosis of MNG, since there are no specific symptoms of MNG, in the early stages of the disease it is mostly asymptomatic, and the available clinical manifestations in most cases are caused by concomitant pathology.

Knowing the stage of the disease is necessary for choosing the optimal treatment tactics. The examination and treatment plan is built taking into account the main ways of tumor spread (hematogenic and lymphogenic metastasis, germination in surrounding organs, intra-abdominal dissemination). Some research methods allow primarily to detect distant metastases (for example, laparoscopy), others to assess the locoregional spread of the disease (endoulttrasound), others combine both possibilities (ultrasound, CT, magnetic resonance imaging - MRI).

Given the fact that in Ukraine, early gastric cancer is diagnosed rather by chance, scientists emphasize the need for a targeted policy on the formation of public opinion, focused on the need for early, active detection of gastric cancer, as well as the organization of dynamic dispensary monitoring of patients of risk groups and persons who have "stomach" complaints, including planned fibrogastroscopy as a screening method: for practically healthy persons over the age of 45-50 - 1 time in 2 years, and in the elderly 50-69 years - 1-2 times a year.

Conclusions. Despite the fact that the role of infectious agents and genetic disorders in the pathogenesis of MNG has been proven, it is a polyetiological disease, in the occurrence and development of which risk factors play an important role: behavioral (harmful eating habits, alcohol abuse, tobacco smoking), social and psychological (chronic stress), socio-economic (low income and level of education associated with poorer access to medical care and awareness of risk factors), professional (harmful production factors), environmental (environmental pollution and introduction of carcinogens into the body through food, water, air), medical (precancerous gastric diseases) and others, most of which are manageable.

The positive results of gastric cancer treatment directly depend on the timeliness of its recognition and clarification of the degree of spread of the tumor process, which allows choosing the optimal treatment tactics.

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