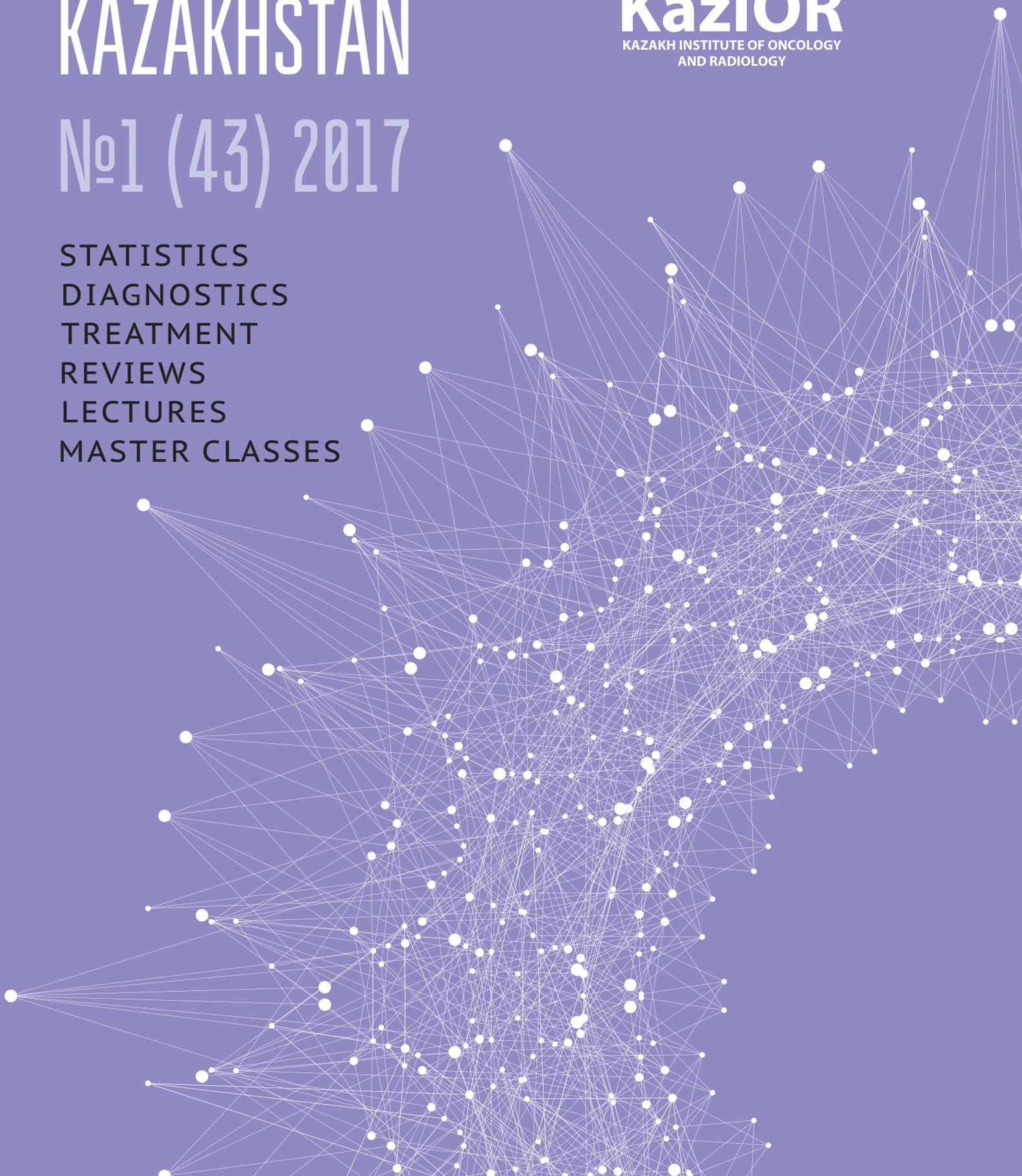


ONCOLOGY and RADIOLOGY of KAZAKHSTAN

№1 (43) 2017



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ONCOGYNECOLOGY

UDC: 616.146-006.6

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Strategy of cervical cancer primary and secondary prevention

The lack of screening programs and high prevalence of human papilloma virus (HPV) are the major factors of high risk of cervical cancer (CC) in low-income and developing countries. The discovery by Harald zur Hausen of connection between chronic persistence of oncogenic HPV (high-risk HPV) and the development of CC marked the beginning of the organization of primary prevention of CC through the creation of vaccines against high-risk HPV, and the development of HPV testing as an emerging strategy for secondary prevention of cervical cancer.

Keywords: cervical cancer, human papilloma virus, screening, vaccination.

Relevance. Cervical cancer (CC) is one of the most common cancers. It ranks fourth among female cancers and seventh among all malignant tumours. 528,000 new cases of CC were registered during 2012. East Africa (42.7 per 100,000), South Africa (31.5 per 100,000), and Latin America (20.0 per 100,000) have high incidence of CC – more than 30 cases per 100,000 [1]. North America (10.2 per 100,000), Western Europe (8.0 per 100,000), Australia (5.5 per 100,000), New Zealand (5.5 per 100,000), and West Asia (4.4 per 100,000) have the lowest incidence rates [1].

Despite the introduced preventive measures, the mortality remains high. In 2012, Globocan reports about 445,000 deaths related to this disease, with the most part of it (230,000) – in low-income countries. The highest mortality was in East Africa (27.6 – more than 20 cases per 100,000 [1].

Human Papilloma Virus

The human papilloma virus (HPV) is the causative agent of CC [3]. This family of heterogeneous viruses includes more than 200 genotypes; more than 40 types of HPV are transmitted sexually. [4]. Fourteen of HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) are pathogenic or «of high risk» and foster the CC [5, 6].

Although most of the sexually active women get infected with HPV once in life [7], less than 10% of women get chronically infected [8]. Such «chronic» infection with a highly oncogenic HPV genotype contributes to CC [8-10].

The HPV particles were first visualized in the middle of 1900s; in the late 1990s the oncogenic genotypes of HPV were named as a major risk factor for CC. HPV virology is important for understanding the CC development.

HPV belongs to the family of papilloma viruses. Its classification has a clinical significance for the following reasons: (1) only one specific HPV genus is associated with CC; (2) different HPV genotypes have different pathogenicity. HPV are grouped into five genera (α , β , γ , μ and η). A-HPV includes HPV genotypes which

infect both the genitals and the oral mucosa [11]. HPV is also grouped in «high risk» and «low risk» categories based on their oncogenic potential. Among the 14 high-risk HPV genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68), the two most common types – HPV 16 and 18 – are responsible for 71% cases of CC [12]. Two low-risk HPV types (6 and 11) contribute to the formation of pointed condylomas most of which require specialized treatment [12].

According to the US Centres for Disease Control and Prevention (CDC), about 6.2 million new cases of HPV are registered each year in the US, with about 20 mln people infected today [13]. It is sexually transmitted and widely spread among all sexually active groups of population. The CDC believes that at least half of all sexually active people will be infected with HPV at a certain moment; at that, at least 80% of women are infected at the age of 50 [13]. In the US, 10% of the population has an active HPV infection; in 4%, the infection has caused cytological abnormalities; and in another 1% it has caused genital condylomas [14].

The peak incidence of HPV infection is observed in juniors and adolescents, with 80%-90% probability of infection. The HPV incidence decreases with the age. HPV infection persists in 5%-15% of infected women, while 85%-90% of infections become laboratory-undetectable within two years [15]. Chronic persistence of HPV 16 and 18 causes 70%-75% of CC cases [16]. HIV-infected women are at higher risk of recurrent HPV infection despite ongoing antiretroviral therapy and have a higher risk of cervical neoplasia.

The carcinogenesis in CC includes four stages: the HPV infection of the cervical transformation zone, the persistence of infection, the increase and transformation of HPV infected cells into the cervical intraepithelial neoplasia (CIN III) or adenocarcinoma in-situ (AIS), and progression into an invasive cancer [17]. Minor cell abnormalities, such as abnormal squamous changes of unclear significance (ASCUS), low-grade squamous intraepithelial lesions (LSIL) or abnormal glandular changes in indeterminate significance (AGUS) in cytological smears, or cervical intraepithelial low-grade lesions (CIN I) in histological response may be observed within several months after infection with HPV [17]. With untimely treatment, 40%-50% of CIN III and AIS cases can progress to cervical cancer within 5-30 years [16, 18, 19]. The time between HPV infection and the development of CIN III is shorter than the progression of CIN III to invasive cervical cancer. Despite the improvement of socio-economic status, awareness of the population, the empowerment of women in the fields of education and science, healthy lifestyles, and improved hygiene which promote the reduction of risk of CC, the preventive vaccination of teenage girls against HPV before their first sexual

contact is an economically beneficial and effective primary prevention strategy [20, 21].

Prevention of Cervical Cancer.

The awareness of the chronic infection with high-risk HPV being the reason of almost all cases of CC has led to the development of primary and secondary CC prevention strategy. The strategy includes primary prevention by vaccination of teenage girls before their first sexual contact to prevent HPV infection, and secondary prevention through the detection of precancerous lesions of cervix, such as CIN III and AIS by screening & HPV testing of women above 30 years. Two recombinant HPV vaccines available today – a four-valent HPV vaccine against types 16, 18, 6, and 11; and a bivalent vaccine against HPV types 16 and 18 – contain real viral particles [22]. Both vaccines showed high immunogenicity and significant protection against chronic HPV infection, CIN III, and intraepithelial neoplasia of the anus for women aged 15-26 [22]. In the vaccinated population, both vaccines protect against 70% of cases of CC [25]. The efficacy of vaccines against persistent infection, investigated in phase III clinical trials, exceeded 99% [22]. The vaccine studies showed strong enough immunogenicity and excellent safety in adolescence, although clinical trials did not include girls below 9 years old who are the main target group of the national vaccination program [22]. Evidence on vaccine safety and efficacy in clinical trials, as well as public health guidelines recommend the inclusion of HPV vaccination in the national immunization programs. The most common adverse reactions following vaccination against HPV included pain at the injection site from mild to moderate, headache and fatigue [20].

Vaccination against HPV targeting mainly teenage girls is now a part of the national immunization program in 62 countries [20, 21, 23]. The research on cost-effectiveness supports the vaccination of teenage girls against HPV before their first sexual contact, also in the low-income and developing countries, subject to the availability of vaccines; the cost-effectiveness of vaccination largely depends on cost per HPV vaccine [24, 25]. Even with a significant reduction in the cost of vaccines over the past few years, the cost of vaccines remains a serious problem for low-income countries. In terms of the economic benefits of vaccination, the efficacy and safety of vaccines, the government shall consider the inclusion of a two-dose vaccination against HPV in the national immunization program in developing and low-income countries that can implement this program at affordable prices through multi-level pricing, as well as through the Gavi vaccine alliance or the PAHO (Pan American Health Organization) foundation.

The vaccination of 58 million of 12-year-old girls in 179 countries worth \$ 4 B shall prevent 690,000 cases of CC and 420,000 deaths. The vaccination against HPV (adjusted for annual disability and taking into account the cost of GDP per capita) was considered economically efficient in 156 (87%) out of 179 countries [21]. Still, various studies recommend different optimal age for teenage girls' vaccination [26]. Some studies also substantiate the vaccination of boys against HPV [20, 27].

The immunogenicity after two-dose vaccination of teenage girls was close to the three-dose regimen with a proven efficacy against persistent infection and precancerous lesions [28-32]. As the immune effect of two doses for 9-14 year-old girls was

comparable to the effect of three doses, the EMA and 10 countries in Central and North America, Africa and Asia got a license for a two-dose vaccination regimen. Canada, Chile, Colombia, Mexico, South Africa, the UK and Switzerland now use a two-dose regimen, while most of the national immunization programs include a three-dose regimen.

In some developed countries, where vaccination was introduced four or five years ago, the preliminary assessment of HPV vaccination programs showed a notable reduction of HPV infection, genital lesions associated with HPV infection, and cervical precancer in the vaccinated population [33-35]. In April 2007, Australia introduced a quadrivalent HPV vaccine for girls aged 12-13 years. More than 70% of the main target group was covered with a three-dose vaccination regime.

The incidence of HPV types 16/18/6/11 has decreased by 77% after the inclusion of HPV vaccination in the national program. In the vaccinated target age group of Australia, the development of condylomas acuminates has decreased by 90%, the CIN III and AIS – by 48% [33, 36]. The population cross-sectional study in Scotland has shown a significant reduction in the prevalence of HPV types 16 and 18 among HPV vaccinated women: 13.6% compared to 29.5% among unvaccinated women [38]. Since the introduction of HPV vaccination in Denmark in 2006, the risk of atypia, or CIN II-CIN III, has decreased among vaccinated women significantly – by 44% [34].

Among the female population of Kazakhstan, CC ranks second after breast cancer. 2 women die from CC daily what causes a significant economic harm to the national economy.

Since 2005, preventive examinations take place in women's health consulting rooms all over the country. In 2008, the order of the Ministry of Health of the Republic of Kazakhstan No. 607 was issued «On the improvement of preventive examinations of certain categories of adult population»; the order No. 665 of 2009 «On Approval of the Rules for Conducting Preventive Medical Examinations of Target Populations» was reissued on 29.12.2014 under № 361. Since 2008, there is a national CC screening program using PAP test and Bethesda classification. [37]. All women aged 30 to 60 years are screened every 5 years. The program was introduced in stages starting from training of specialists, arrangement of women's health consulting rooms and their fitting with vaginoscopes [38]. Liquid cytology was actively introduced since 2011 to provide a number of advantages vs. the traditional method. It is a quick method of investigation and easy way to obtain samples; it also highly sensitive for mild and severe pathologies.

Conclusion. Today, WHO recommends a two-dose vaccination regimen for girls with a minimum interval of six months between doses if the vaccination starts before the age of 15 [34]. This recommendation increases availability of HPV vaccination more affordable in comparison to the three-dose regimen. A three-dose regimen of 0, 1-2 and 6 months is required for girls not vaccinated till the age of 15, as well as for people with weakened immune systems, including HIV infected people. As far as HPV vaccination reduces the prevalence of infection and the development of cervical neoplasia, the screening will reduce mortality from CC among women not vaccinated against HPV. The long-term impact of vaccination on the CC screening will be country-specific and will

depend on immunization, coverage of vaccination, the impact of population immunity, and the starting age for screening.

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GASTRIC CANCER

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Gastric cancer incidence and mortality dynamics in Kazakhstan in 2004-2014

Kazakhstan has a high incidence and mortality of gastric cancer (GC). Epidemiological analysis of GC prevalence in Kazakhstan during 2004-2014 was conducted for the purposes of monitoring and assessment of cancer care, treatment and preventive measures. Primary GC incidence and mortality have decreased from 22.3‰ to 17.2‰, and from 18.7‰ to 12.9‰, respectively (standardized WHO World indices). GC incidence in men was 2.5 times higher than in women. Several regions like Pavlodar, Kyzylorda, Aktobe, and Akmola had a high GC incidence. In 2009-2014, the incidence has increased in Astana, Zhambyl, Akmola, Aktobe regions, with a decrease in North Kazakhstan and Mangistau regions. The proportion of stages I-II increased by 1.8 times. The ratio of mortality to incidence for the period has decreased from 83.9% to 66.6% what indicates an improvement in cancer care in the Republic of Kazakhstan. The revealed features of GC incidence and mortality in the Republic of Kazakhstan will be taken into account during further expansion of screening and long-term planning of treatment and diagnostic measures.

Keywords: gastric cancer, morbidity, mortality, the Republic of Kazakhstan.

Introduction. The incidence of gastric cancer (GC) is high in different countries worldwide. GLOBOCAN reports 951 594 cases of gastric malignancies in 2012, with 723 073 fatal cases [1]. The average world morbidity was 12.1% (17.4% in men, and 7.5% in women) – No. 6 among all cancers. The mortality was 8.9% (12.8% in men, and 5.7% in women) – No. 4 among all cancers. Mortality to morbidity ratio was 73.6%.

Materials and methods. The target of research was the updated information obtained from the «Reports on cancer morbidity» and «Reports on patients with malignant neoplasms» (Form No.7 and Form No.35 approved by the Order of the Minister of Health of the Republic of Kazakhstan № 128 of March 6, 2013) for 2004-2014, information from the «Notification about a patient with a primary cancer or another malignant neoplasm» (Form No. 090/u approved by the Order of the acting Minister of Health of the RK № 514 of July 31, 2012), and the data of the Committee for Statistics of the Ministry of National Economy of the RK on the number and sex and age composition of the population of the RK in 2004-2014. In total, 30 699 cases of GC were registered in Kazakhstan in 2004-2014, with 25 013 deaths. The materials were analysed through the Republic, with the account of the administrative and territorial division into 14 regions and two main cities of Republican status – Astana and Almaty. The traditional methods of statistical data processing were applied

[2-4] to calculate the extensive, intensive, standardized and age-specific incidence rates, as well as mortality rates per 100,000. The statistical indicators were calculated using the IARC (International Agency for Research on Cancer) recommended methods [5]. The standardized indicators were calculated using the world standard population of the WHO (World Health Organization) [6]. The status of cancer care was assessed by the indicators of cancer service of the RK for 2008 and 2014 [7, 8].

Results. The incidence rates (per 100,000 standardized by World age structure) varied from 2.2% in Poland and Estonia to 41.8% in Korea (Table 1). Kazakhstan was in the group of countries with high incidence rate. WHO, GLOBOCAN 2012 estimates slightly exceeded the real indicators of the Electronic Registry of Cancer Patients of the Republic of Kazakhstan (ERCP RK). That was due to the methodological calculations used by IARC in the formation of GLOBOCAN 2012 when the national morbidity rates were calculated on the basis of 5-year survival rates [9].

All the countries have shown significant differences in the incidence by sex: men were two or more times more likely to have GC than women. In Kazakhstan, sex differences were also expressed; the incidence among men was 2.6 times higher than in women. The «mortality to morbidity ratio» that characterized the level of cancer care development in a particular country was high in both developed and developing countries. That indicated the seriousness of the problem of radical treatment of GC and its necessary early detection. Low mortality to morbidity ratio was recorded in Japan (41.5%) and Korea (31.1%) while in Denmark, Canada and Estonia those ratios have approached or exceeded 100%. In Kazakhstan, the ratio was 77.8% according to the updated information of the Electronic Register of Cancer Patients of the Republic of Kazakhstan. It should be noted that according to GLOBOCAN 2012, this ratio was worse for Kazakhstan (83.5%). That evidenced some progress in early diagnostics and treatment of that cancer of complicated localization.

The analysis of intensive and standardized indicators of GC incidence (Figure 1) shows a decrease in primary incidence. The primary incidence in 2004-2014 has also reduced from 20.0% to 16.4%. Standardized indicators have a similar pattern of lower incidence. The coefficient of regression of standardized indicators does not differ from the corresponding coefficient of intensive indicators, which indicates the absence of the effect of population aging on the level of morbidity. Reducing the incidence rate also indicates a decrease in the effect of adverse etiologic factors.

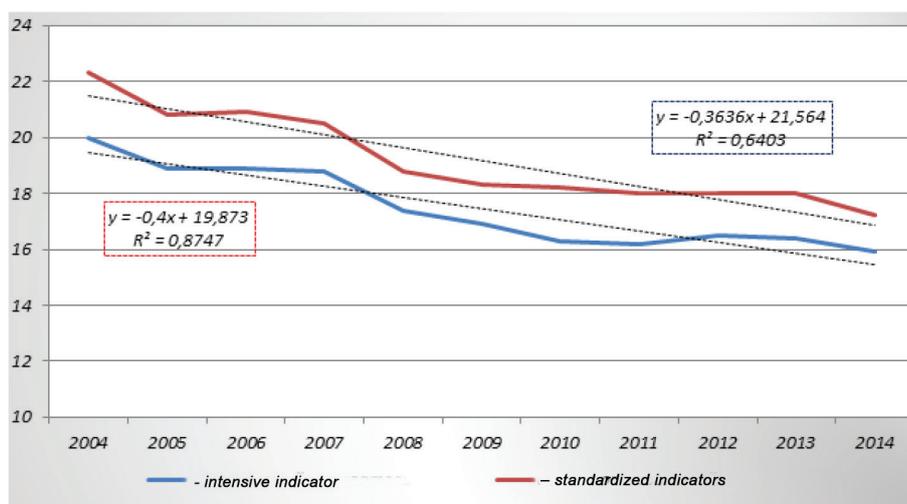
Table 1 – Incidence and mortality of gastric cancer in the selected countries, 2012 (per 100,000, WHO world standard, GLOBOCAN 2012).

Countries	Incidence			Mortality			Mortality to morbidity ratio,%
	Men	Women	Both sexes	Men	Women	Both sexes	
Kazakhstan*	35,25	12,79	21,6	30,4	10,5	18,0	83,5
Kazakhstan**	21,5	11,7	16,5	24,6	9,3	12,8	77,6
Kazakhstan***	28,7	11,1	18,0	22,0	8,7	14,0	77,8
Kyrgyz Republic	6,9	10,27	21,4	33,0	9,5	19,6	91,9
Russian Federation	6,4	0,9	3,1	5,9	0,7	2,7	87,1
Uzbekistan	16,8	8,8	12,5	15,6	8,1	11,4	91,2
Ukraine	5,5	0,5	2,5	4,5	0,3	2,0	80,0
Great Britain	10,0	3,5	6,5	8,7	2,9	5,6	86,2
Germany	6,9	1,3	4,0	4,5	1,1	2,7	67,5
Denmark	5,6	2,4	3,9	6,5	1,9	4,1	105,1
Latvia	7,1	1,0	3,5	6,8	0,7	3,2	91,4
Lithuania	7,6	0,8	3,6	7,4	0,7	3,5	97,2
Netherlands	10,0	2,8	6,3	8,3	2,3	5,2	82,5
Poland	4,0	0,8	2,2	3,8	0,7	2,1	95,5
Slovakia	6,4	0,8	3,4	5,8	0,7	3,0	88,2
Finland	3,7	1,1	2,3	3,0	1,0	1,9	82,6
France	6,1	1,7	3,8	5,1	1,0	2,9	76,3
Switzerland	6,1	1,9	3,8	4,4	1,1	2,6	68,4
Sweden	3,5	1,1	2,3	3,1	0,9	2,0	87,0
Estonia	4,5	0,6	2,2	5,1	0,3	2,2	100,0
Canada	4,6	1,1	2,8	4,6	1,0	2,7	96,4
USA	5,5	1,1	3,2	5,1	1,0	2,9	90,6
China	32,8	13,1	22,7	25,5	10,7	17,9	78,9
Korea	62,3	8,8	41,8	13,6	7,9	13,0	31,1
Japan	45,8	16,5	29,9	18,8	7,3	12,4	41,5
Australia	6,7	3,1	4,8	3,5	1,6	2,5	52,1
Brazil	13,1	6	9,2	10,9	4,6	7,4	80,4

* WHO, GLOBOCAN 2012

** ERCP RK, intensive (crude) indicators

*** ERCP RK, standardized indicators

**Figure 1** - Dynamics of WHO World intensive and standardized incidence rates of GC per 100,000 in the Republic of Kazakhstan in 2004-2014.**Incidence by sex**

The analysis of incidence of GC (Figure 2) revealed a difference by sex. Both in 2004-2008 and 2009-2014, men were 2.5 times more likely to suffer from GC than women. That was an average situation worldwide.

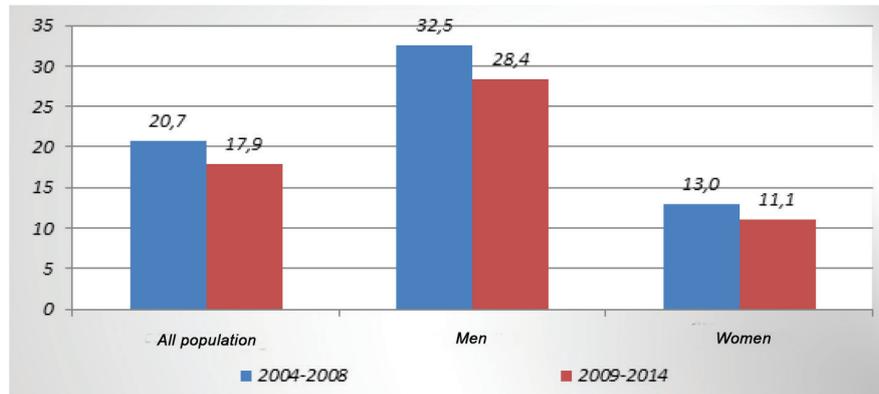


Figure 2 - Incidence of gastric malignancies in the Republic of Kazakhstan by sex (WHO World standards per 100,000, in 2004-2008 and 2009-2014)

Incidence by age

The analysis of age distribution of gastric malignancies (Figure 3) showed an increase of incidence starting from the age of 40 to 44 years, with a steady growth and the maximum rates at the age of 70 both in 2004-2008 and 2009- 2014.

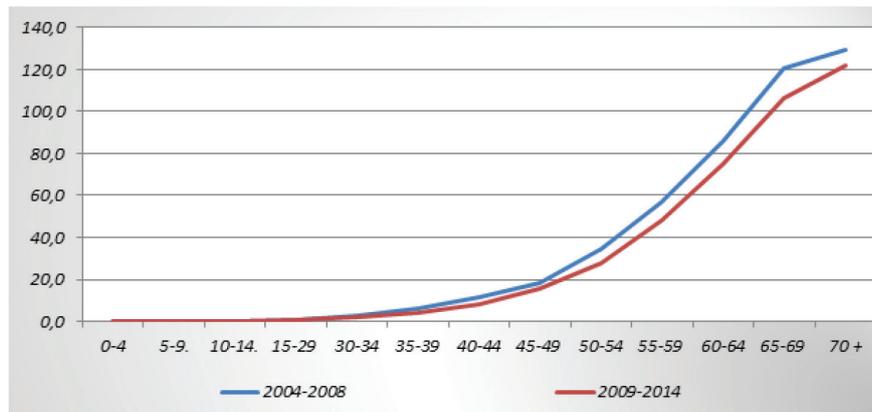


Figure 3 - Age indicators of gastric malignancies in the Republic of Kazakhstan (averages per 100,000 of the relevant age, in 2004-2008 and 2009-2014)

Both sexes had the highest incidence rate at the age of 70 and above, and the age dynamics was similar for both sexes: the incidence rate increased from the age of 40-44 and continued to grow steadily.

Incidence by region of the country

Territorial distribution of gastric malignancies (Figure 4) showed the regions with high incidence (Pavlodar, Kyzylorda, Aktyubinsk, and Akmola regions) while other regions were nearly at the same level. The incidence has notably increased in Astana, Zhambyl, Akmola, and Aktoobe regions in 2009-2014 vs. 2004-2008. In North Kazakhstan and Mangistau region, there was a slight decrease in the incidence in in 2009-2014 vs.2004-2008.

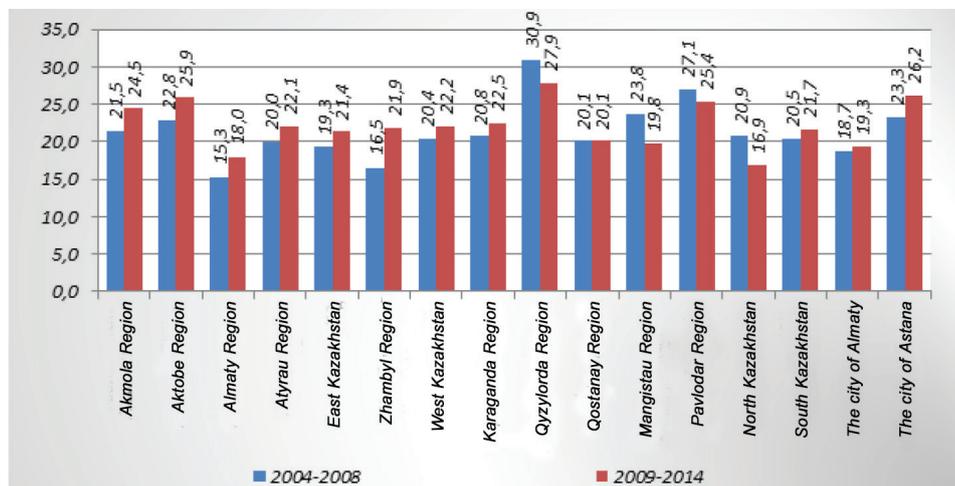


Figure 4 - Territorial rates of incidence of gastric malignancies in the Republic of Kazakhstan (WHO World standardized indicators per 100,000, in 2004-2008 and 2009-2014)

Specific share of stages I-II, III, and IV

In 2004-2014, the share of stages I-II has increased among primary gastric malignancies by 1.8 times (15.7% to 27.6%) whilst the stage IV has decreased from 30.3% to 25.0%, and the stage III – from 51.1% to 44.8% (Figure 5).

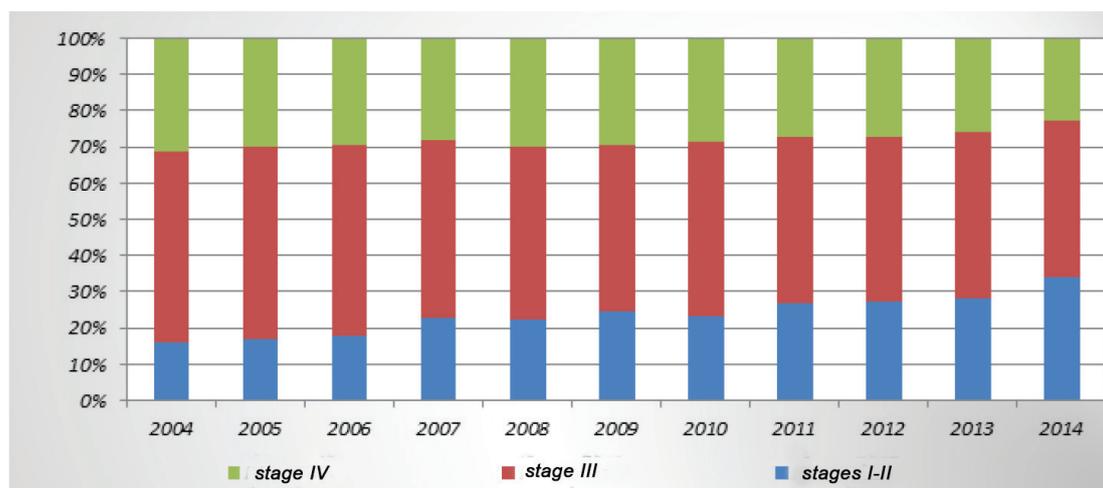


Figure 5 - Specific share of stages I-II, III, and IV of primary gastric malignancies in the Republic of Kazakhstan (%)

The status of cancer care

Table 2 presents the main statistical indicators characterizing the state of cancer care for patients with gastric malignancies [7, 8]. The number of newly registered cases has increased by 2.6% in 2013 vs. 2008; the number of morphological confirmations has increased by 3.7%, and amounted to 87.5%. The share of stages I-II has increased by 5.7% in 2013 vs. 2008. In addition, there was a decrease in the specific share of stage IV by 1.9% to reach 44.8% in 2014. Within-one-year mortality rate has decreased by 6.1% what evidenced the improvement in timely diagnostics of gastric malignancies. The number of patients receiving radical treatment has increased by 6.3% to reach 37.9%. The changes in 5-year rates are minor. Moreover, the increase in the share of late stages compared to the early stage of GC by 2.1 times in 2008 and 1.6 times in 2013 witnesses the seriousness of the problem of early diagnostics of GC.

Table 2 - Main statistical indicators of gastric cancer

Indicators	2008	2013
Number of primary cases	2726	2796
Morbidity per 100,000 (crude intensive indicator)	17.4	16.4
Morbidity per 100,000 (WHO World standardized indicator)	18.8	18.0
Share of stages I-II (% of primary cases)	21.9	27.6
Share of stages IV (% of primary cases)	46.7	44.8
Number of primary cases detected at screening	85	193
Detection rate of screening (% of examined)	3.1	6.9
Morphologically verified (% of detected)	83.8	87.5
Less than one year survival from the moment of diagnosis, of those registered last year (within-one-year mortality rate, %)	57.5	51.4
Radical treatment required (% of newly ill who received complex treatment)	31.6	37.9
Deaths from gastric malignancies	2251	2129
Mortality per 100,000 (crude intensive indicator)	15.2	14.6
Mortality per 100,000 (WHO World standardized indicator)	16.5	16.5
Mortality to morbidity ratio, % (intensive indicators)	87.4	89.0
Mortality to morbidity ratio, % (standardized indicators)	87.8	91.7
Patients registered by the end of the year	6584	6075
Of them, registered for 5 years and more (%)	40.5	45.3

In 2004-2014, the mortality rate was decreasing: the intensive indicators – 16, 7% to 11.9%, the standardized indicators – 18.7% to 12.9% (Figure 6). The “mortality to morbidity ratio» was changing wavyly, with increases (up to 87.8% in 2008) and decreases in different years. In fact, in 2004-2010 the mortality to morbidity ratio was stable at the level of 85%. Since 2010, it was steadily decreasing confirmed by quite high regression factor $R^2 = 0.6507$. During that period, the age-standardized mortality and incidence has decreased up to 66.6% in 2014 what was comparable to such countries as Germany and Switzerland [1].

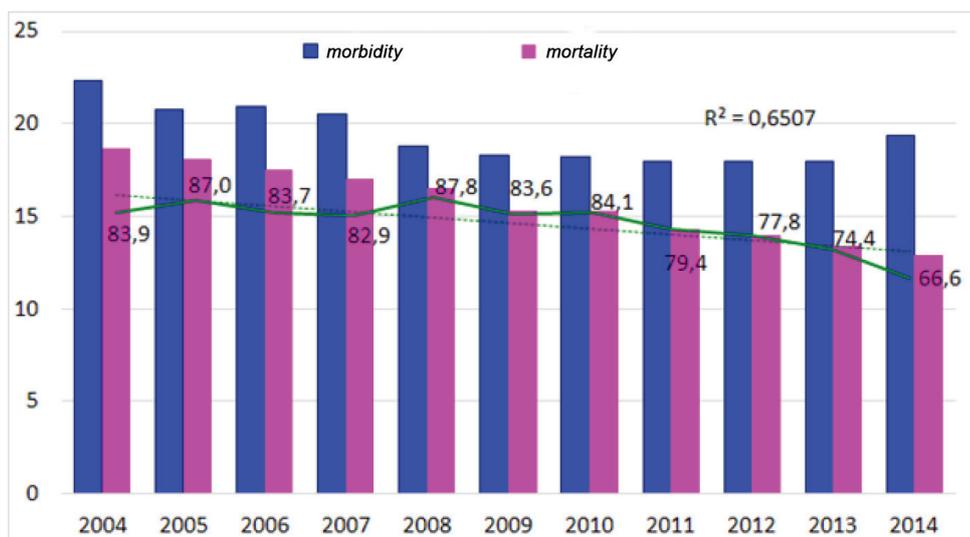


Figure 6 - Gastric malignancies: incidence, mortality (intensive indicators), mortality to morbidity ratio (%), in 2004-2014

In order to reduce mortality from GC, endoscopic screening was introduced in a pilot mode since 2013 aimed at early detection of oesophageal cancer and GC. Currently, screening is carried out in 11 regions of Kazakhstan every 2 years and covers about 330 thousand men and women from 50 to 60 years. 50% of target population is covered annually. There are certain problems with the implementation of this screening but even during the first years of screening the incidence of GC in 2014 has increased – for the first time in more than 10 years. The mortality from GC started decreasing only after 2010.

Conclusions. The analysis of GC prevalence in Kazakhstan shows a stable and still unfavourable situation. Only in the last 5 years there are some slightly positive trends: a decrease in mortality that is more evident in intensive indicators, an increase in the share of early stages, and a decrease in the mortality to morbidity ratio. The implementation of the State Program «Salamatty Kazakhstan», the Program for the Development of Cancer Care in the Republic of Kazakhstan, the launch of oesophageal and gastric cancer screening program supported the start of equipping of outpatient clinics with modern endoscopic equipment, the training of staff, promoted raising the awareness of population about oncologic alarm and early cancer diagnostics. The revealed peculiarities of GC incidence and mortality in the Republic of Kazakhstan shall be taken into account during long-term planning of therapeutic and preventive measures, the expansion and evaluation of quality of oesophageal and gastric cancer screening.

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Capabilities of computer tomography in gastric cancer diagnostics

Early diagnostics of gastric cancer (GC) remains a vital problem of today. This study was done to define the relevance and potential of computer tomography (CT) in diagnostics of GC. The study group consisted of 59 patients at the mean age of 59.8 with primary diagnosed GC. They underwent CT before surgery to determine the prevalence of the process. The CT results were analyzed by the process localization, tumor growth form, visualization of regional lymph nodes, CT-semiology of GC, invasion of the adjacent organs, and the presence of distant metastases. The CT showed the prevalence of endophytic GC growth form (46 cases, 78%) over the mixed (11, 19%) and exophytic forms (2, 3%). In most cases, GC was observed in the stomach body (49%). The augmentation of regional lymph nodes was revealed in 47.4% of GC cases. The adjacent organs were invaded in 5 (8.5%) cases, with liver metastases in 2 (3.4%) cases. In 11.9% of cases, CT allowed to review the stage of the process and treatment strategy.

CT is the method of choice for the staging of gastric cancer.

Keywords: computer tomography, gastric cancer.

Relevance. Gastric cancer (GC) ranks five in the world among other cancers. 951,000 new cases of GC were registered in 2012 accounting for 7% of all malignances. GC is the third cause of cancer mortality worldwide after lung and liver cancers [1, 2]. In 2014, GC ranked fourth in Kazakhstan among all cancers and second in the structure of cancer mortality [3]. GC has a high recurrent rate and a low five-year survival index worldwide (about 25-30% in 2012), as well as in Kazakhstan (46% in 2014).

Early diagnostics of GC remains a vital problem of today. The main diagnostic technique is esophagogastrosocopy followed by biopsy [5]. The radiological methods of GC diagnostics include X-ray imaging, stomach CT or MRI [6]. Standard 2D-mode CT programs provide only 20-56% sensibility of CT in GC diagnostics therefore today CT is not used for primary radiological diagnostics of GC but is the method of choice mainly for the staging of GC [5].

The presented study was done to define the potential of CT in diagnosing the GC.

Material and methods. 122 patients with histologically verified malignant neoplasm of stomach underwent stomach CT in Kazakh Institute of Oncology and Radiology from Jan. 01, 2015 till Nov. 01, 2016. Of them, 63 (51.6%) patients with previously established GC passed CT repeatedly so they were not included in the research.

The study group consisted of 59 patients at the mean age of 59.8 with primary diagnosed GC. All patients previously underwent esophagogastrosocopy followed by biopsy and were diagnosed with GC. They underwent CT before surgery to determine the prevalence of the process. The CT results were analyzed by the process localization, tumor growth form, visualization of regional lymph nodes, CT-semiology of GC, invasion of the adjacent organs, and the presence of distant metastases.

The examination was done using the computer tomographic scanner LightSpeedVCT (GE) with oral and intravenous administration of a contrast agent (visipack, ultrawhist). The CT research was conducted in the axial plane with the subsequent re-formatting in the sagittal and frontal planes.

Results. The CT results were analyzed by the process localization, tumor growth form, and visualization of regional lymph nodes. Figure 1 provides the distribution of GC cases by growth form according to CT.

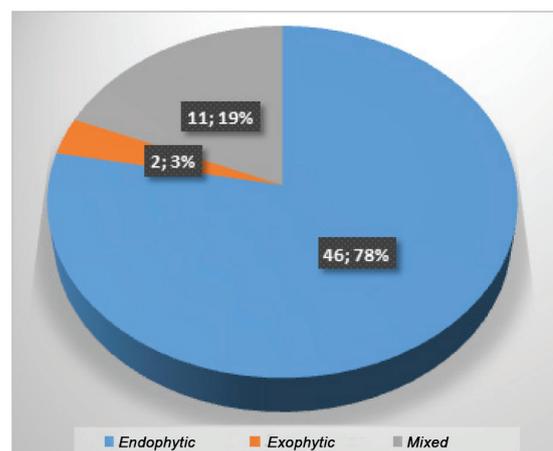


Figure 1 - Distribution of GC cases by growth form according to CT

As shown in Fig. 1, endophytic growth form (46 cases, 78%) prevailed over the mixed (11, 19%) and exophytic forms (2, 3%).

Figure 2 shows the distribution of GC cases by localization of the process according to stomach CT.

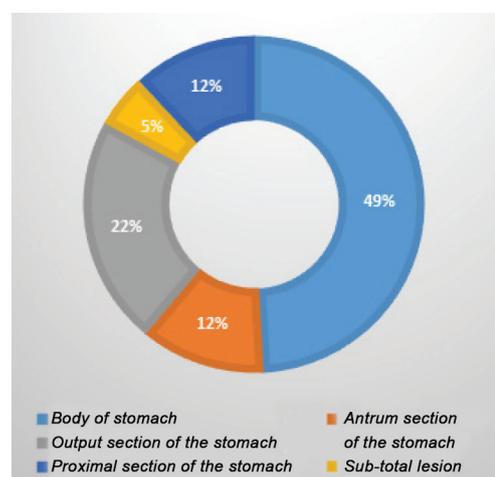


Figure 2 - Distribution of GC cases by process localization according to CT

In most cases, GC was localized in the stomach body (49%). Localization in the pylorus was 2.2 times less often (22%), even more rarely - in proximal section (12% cases), with the least number of cases in antral section (5%). Subtotal lesion of stomach was observed in 12% of cases.

Figure 3 provides the results of analyses of enlarged regional lymph nodes in GC patients on CT-slices.

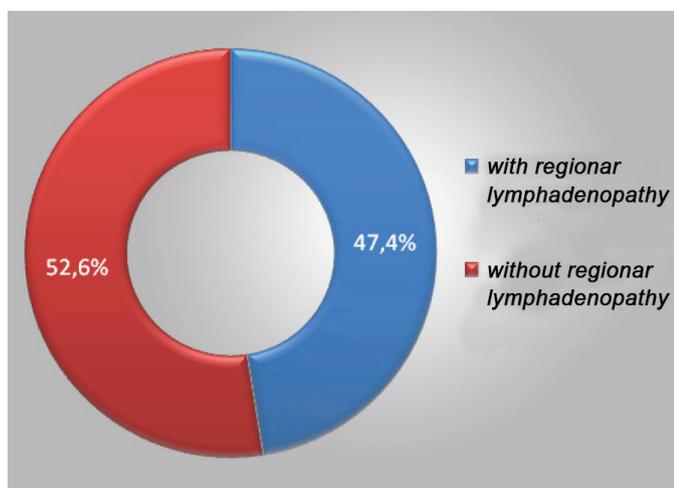


Figure 3 – Involvement of regional lymph nodes during GC according to CT

The CT of stomach and abdominal organs showed the augmentation of regional lymph nodes in 47.4% (28) of GC cases. In 52.6% of cases, the lymph nodes were not visualized.

CT semiology of GC was studied to analyze the frequency of the following symptoms on CT-slices of GC patients: the thickening of the stomach wall, the pathological reorganization of relief, the unevenness and blurring of stomach contours. All 59 (100%) patients had thickened stomach walls, the unevenness and blurring of stomach contours was observed in 41 (69.5%) cases while the

pathological reorganization of relief was rare on CT-slices and was found only in 9 (15.3%) cases. The maximum thickness of stomach wall at GC reached 3.2 cm according to CT.

The stomach CT allowed analyzing invasion of gastric tumor process in adjacent organs and the presence of metastatic process in the abdominal organs, retroperitoneal space and bone structures. The adjacent organs were invaded in 5 (8.5%) cases, with liver metastases in 2 (3.4%) cases.

Conclusion. In 11.9% of cases, CT allowed to review the stage of the process and treatment strategy. CT is the method of choice for the staging of gastric cancer.

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Vascular endothelium dysfunction in patients with gastric cancer and its correction

122 patients with gastric cancer of clinical stages II and III were comprehensively examined after radical surgery to define the efficiency of this endothelial dysfunction correction method. Functional performance of endothelium and circulating endothelial content were tested to reveal that the treatment with L-arginine and ACE inhibitor had mitigated endothelial dysfunction and endothelial damage. It correlated with a reduced frequency of postoperative complications, late complications in the form of recurrence and metastasis, and mortality.

Keywords: gastric cancer, endothelial dysfunction, correction, clinical outcome.

Introduction. Endothelial dysfunction is a universal mechanism for development of pathological processes. It affects the course and outcome of all forms of human diseases [1, 2]. In malignant neoplasms, endothelial factors influence the development of tumours by producing the factors of vascular growth which determine the neovascularization of the neoplasm [3, 4].

Other endothelial mechanisms may be important in both pathogenesis and treatment of tumours, i.e., they can influence the systemic and local circulation and haemostasis [5]. The outcome of cancer diseases is known to be often determined by concomitant pathology which progression is associated with neoplasia or with the risk of thrombosis [6].

Both aspects are very important in surgical treatment of cancer since the intervention intensifies endothelial dysfunction and stimulates the associated pathophysiological changes.

The existing methods of drug-induced correction of endothelial function in oncology influence only the vascular growth factors but not the vasomotor and prothrombotic mechanisms. We believe that the normalization of the latter will reduce the risk of postoperative complications and improve the course of rehabilitation period.

The purpose of the study is to determine the effect of correction of endothelial dysfunction by the combination of L-arginine and the angiotensin-converting enzyme inhibitor in postoperative patients with gastric cancer (GC).

Materials and methods. A comprehensive examination of 62 patients with GC stage II and 60 patients with GC stage III (altogether, n=122), of them, 87 men and 35 women, aged 41 to 70 years old (average age 64.2 ± 2.3 years) was performed.

All patients underwent surgical gastrectomy or subtotal resection of stomach with D2 lymph dissection.

Severe concomitant somatic diseases were the exclusion criteria. The mandatory inclusion criterion was the informed consent of patients for additional methods of conservative therapy and the anonymous use of obtained results in a scientific study.

All patients were divided into two groups by the use of additional perioperative therapy aimed at the correction of endothelial dysfunction (treatment arm n = 54, comparison arm n = 68). The patients in different groups had no significant discrepancies in terms of age, sex, stage of neoplasm, tumour localization in the stomach, the severity of condition in preoperative period, the concomitant diseases and the conducted surgical interventions.

The control arm included 40 practically healthy individuals aged 40 to 65 (mean age 57.3 ± 2.0 years).

The studied indices of vascular endothelial function included: the content of desquamated (circulating) endotheliocytes in the blood (CE), the concentration of von Willebrand factor (vWF) in plasma and the degree of endothelium-dependent vasodilation (EDVD) [7].

Clinical results were reviewed to detect purulent-septic, thrombotic complications early postoperatively and prospectively (2.1 ± 0.1 years in the treatment arm and 2.0 ± 0.2 years in the comparison arm).

Additional therapy aimed at the correction of endothelial dysfunction included L-arginine (vasoton, Barnaul, R.F.) 1.0 g 1/1 with ACE inhibitor (enalapril) 5 mg 1/1. The therapy started 3-4 days pre-surgery. Contraindication for ACE inhibitor was the expressed arterial hypotension (systolic pressure below 90 mmHg). Patients with such hemodynamics were excluded from the study.

The statistical significance of differences in indicators in groups and in dynamics was estimated by Mann-Whitney [8]. The tables show the medians of numerical series (Me), the values of the 25th and 75th percentile, and the statistical significance (p).

Results. The average values of indicators of vascular endothelium in the treatment arm and the control arm are presented in Table 1.

Both arms showed the deviations in the values of the studied indicators from the baseline values, with a significant co-directional and regular dynamics in early postoperative period. In the treatment arm, the CE content was statistically above the control arm throughout the follow-up period after surgery, with the most significant difference on Day 3 (Me/Me = 4.36, $p < 0.01$).

Differences in the relative incidence of complications in the early postoperative period were RR = 2.05 for the clinical stage II, and RR = 2.38 for the clinical stage III ($p < 0.05$, in both cases). Differences between the treatment arms were more significant in the long-term for the clinical stage II, (RR = 2.34, $p < 0.05$), and in the short term – for the clinical stage III (RR = 1.96, $p < 0.05$).

Table 1 – The dynamics of indicators of the state of vascular endothelium in postoperative GC patients

Indicator	Patient arms																													
	Treatment arm						Comparison arm																							
	CE, content per 10 ³ platelets			vWF, %			EDVD, %			CE, content per 10 ³ platelets			vWF, %			EDVD, %														
	П25	Me	П75	Р _{о-с}	П25	Me	П75	Р _{о-с}	П25	Me	П75	Р _{о-с}	П25	Me	П75	Р _{о-с}	П25	Me	П75	Р _{о-с}	П25	Me	П75	Р _{о-с}						
Control arm	1,9	2,2	2,5	-	43,6	51,7	62,8	-	14,0	18,6	23,0	-	1,9	2,2	2,5	43,6	51,7	62,8	14,0	18,6	23,0	1,9	2,2	2,5	43,6	51,7	62,8	14,0	18,6	23,0
Pre-surgery (1) P	4,3	7,7	10,7	>0,05	65,3	76,2	105,1	>0,05	10,0	14,5	17,0	>0,05	4,5	8,1	10,5	64,8	91,9	103,2	9,0	13,6	15,0	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05
Post-surgery (Day 1) (2) P P ₁₋₂	5,2	9,2	12,6	<0,05	79,5	94,8	117,0	>0,05	9,1	12,2	14,9	>0,05	7,3	12,9	16,1	82,5	119,6	128,6	5,7	9,6	11,9	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05
(3) Day 3 P P ₁₋₃ P ₂₋₃	5,5	9,6	13,0	<0,05	79,5	92,5	111,3	<0,05	9,6	13,8	15,3	<0,05	11,2	16,5	19,8	93,7	125,2	134,0	5,5	9,0	11,2	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05
(4) Day 7 P P ₁₋₄ P ₂₋₄ P ₃₋₄	3,8	6,1	8,5	<0,05	51,3	66,4	75,8	<0,05	10,5	15,0	19,2	>0,05	8,6	13,0	17,0	77,1	108,5	117,3	6,8	10,4	13,7	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05

Note: P – the statistical significance of the difference with the control arm; Pn-n – the statistical significance of differences in one group of patients in the dynamics; Po-c - the significance of the differences between the treatment arm and the comparison arm

Day 7 showed a significant downward trend ($p < 0.05$), with a reduction in difference with the control arm up to $Me/Me = 2.77$ ($p < 0.01$). The vWF factor was significantly exceeded at the time pre-operatively and 1 day after ($Me/Me = 1.83$, $p < 0.05$). Later the indicator median was decreasing; on Day 7 the differences with the control arm were less than at the outcome of the study ($Me/Me = 1.28$, $p < 0.05$).

The EDVD level was below the control during the whole study, with no significant dynamics post-surgery. The lowest EDVD level was recorded 1 day after surgery ($Me/Me = 1.52$, $p < 0.05$), the highest level – on Day 7 ($Me/Me = 1.24$, $p > 0.05$).

Patients with GC had substantial and statistically significant differences in the CE content post-surgery associated with the specifics of treatment. 1 day after surgery, the CE content was higher in the comparison arm vs. the arm of L-arginine (the treatment arm) ($Me/Me = 1.40$ ($p < 0.05$)). On Day 3, the difference increased to $Me/Me = 1.72$ ($p < 0.05$), on Day 7 – to $Me/Me = 2.13$ ($p < 0.01$). The vWF factor was higher in the comparison arm vs. the

treatment arm throughout the study. The statistically significant differences were registered 3 days post-surgery ($Me/Me = 1.35$, $p < 0.05$) and 7 days post-surgery ($Me/Me = 1.63$; $p < 0.05$).

Patients who received large doses of L-arginine had excessive level of EDVD post-surgery. On Day 1, the difference was 1.27 times ($p = 0.05$), with an increase on Day 3 ($Me/Me = 1.53$, $p < 0.05$) and a decrease up to 1.44 44 times ($p < 0.05$) on Day 7. The treatment group had a few cases of EDVD decrease below 10%, and no cases of paradoxical reactions of the vascular endothelium to a hypoxic test (in contrast to the comparison arm). Thus, L-arginine and an ACE inhibitor create conditions for better blood supply, also in the zone of anastomosis. Thereby, the above drugs supported the normalization for each of the studied parameters of endothelial function.

Table 2 presents the results of analysis of clinical indicators depending on the clinical stage and the applied method of conservative therapy.

Table 2 – GC treatment outcome by clinical stage and study arm

Indicator	Clinical stage II				Clinical stage III			
	Comparison arm, n = 33		Treatment arm, n = 29		Comparison arm, n = 35		Treatment arm, n = 25	
	No. of cases, n	%	No. of cases, n	%	No. of cases, n	%	No. of cases, n	%
Complications in the early postoperative period	7	21.2	3	10.3	10	28.6	3	12.0
Relapses and / or metastases	8	24.2	3	10.3	11	31.4	4	16.0

Conclusion. Correction of endothelial dysfunction is used in clinical practice only for patients with cardiovascular pathology. The methods of correction of endothelial dysfunction using beta- adrenergic blockers with the effect of direct donation of nitric oxide were developed and the pleiotropic properties of ACE inhibitors were identified for patients with hypertension and coronary artery disease [9, 10].

Cancer surgery and other surgical interventions cause short-term depreciation of endothelial function due a surgical trauma. However, cancer surgery in contrast to other surgical interventions requires to ensure the blocking of the proliferation of neoplastic cells by systemic mechanisms of the macro organism [6, 11]. One of the leading mechanisms is endothelial. An expressed endothelial dysfunction can contribute to the preservation of the tumour cell pool and the possibility of relapses and metastases.

The detected postsurgical deterioration of the functional state of vascular endothelium in GC patients against the background of the initial dysfunction could be the basis for more than 20% of negative results in that group of patients.

The used method of correction of endothelial dysfunction with L-arginine and ACE inhibitor has significantly improved the studied parameters what was in line the clinical efficacy of that method of treatment.

In general we see the prospects for this direction of cancer surgery and oncology in improving the conditions of postoperative patients.

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Modern strategy of surgical treatment of gastric cancer

The article reviews the epidemiology and modern strategy of surgical treatment of gastric cancer by using extended lymph node dissection techniques. The authors present the results of surgical treatment of 348 patients with gastric cancer by extended lymph node dissection.

Keywords: gastric cancer, surgical treatment, lymph node dissection.

Introduction. By the early 20th century, the incidence of gastric cancer (GC) has declined in nearly all the mature countries; this trend remains even in the regions with a high risk of GC. The reason for this might be the change in the diet, the conditions of food storage and cooking [1, 2]. Still, GC remains one of the main causes of death from malignant neoplasms nearly worldwide.

The incidence of GC is quite disputable both in the world and within the countries. Thus, Japan, Korea and China have the highest incidence of GC, while in the US this disease is extremely rare. In Russia, the average incidence is 38.9 per 100,000, with more than 160 per 100,000 in the High North.

In the Republic of Kazakhstan, GC for many years ranks second among all malignant tumours after lung cancer, with the incidence rate of 20.4 per 100,000. Qostanay Region, North Kazakhstan, Kyzylorda Region, East Kazakhstan, and Atyrau Region have incidence rates above the average [3].

Epidemiology of GC. The comparative analysis of regions with high and low incidence allows suggesting some possible etiological factors of GC.

The reliable association of GC with genetic factors is currently disputed [2] while environmental factors have a more significant impact. The analysis has shown a reduction in the risk of GC when moving from regions with a high incidence to the areas with lower incidence, with a more notable reduction in the next generation [4, 5].

The most powerful exogenic factor is the diet. High-calorie food including meat, smoked products, a high concentration of salt is associated with a high risk of GC. In contrast, the consumption of fresh fruits, fiber and vitamins is a protective factor against GC (especially, the intestinal type of cancer) [6].

The association of *Helicobacter pylori* (HP) with GC has been recently proven. The infectious carcinogenesis is associated with the ability of the microorganism to induce a pronounced infiltrative gastritis with intensive cell proliferation. A long period of inflammation causes atrophy and intestinal metaplasia which should be interpreted as precancerous changes of intestinal type. HP is also associated with a 100% of cases of diffuse-type GC [6].

Surgical treatment policy. Despite of some successes in combined treatment, the synthesis of new

chemotherapeutic agents, surgery remains the only method promising a recovery or long-term remission for GC. The radical nature of any cancer surgery was always assessed not only by adequate resection of the organ, but also by monoblock removal of regional lymphocytes as pathways for lymphogenous metastasis. The term of «lymphadenectomy» meaning the removal of a region of possible metastasis is known for more than a century. Recently more and more scientists are inclined to the concept of «lymph node dissection» as it is more capacious than lymphadenectomy and involves the removal of the entire lymphatic apparatus with surrounding cellular tissue.

Many studies have demonstrated a high degree of lymphogenous metastasis of GC as one of the most aggressive GIT tumours. Therefore the need to perform lymph node dissection as one of the main stages of GC surgery is no doubt, both in therapeutic and preventive purposes.

The extended lymph node dissection is pre-conditioned by:

- the improvement of local control in order to reduce the risk of loco-regional recurrence;
- the ability to determine the real prevalence of tumour process and the formation of strategy for post-surgery treatment and prognosis.

Modern literature describes only a few randomized studies of extended lymph node dissection in surgical treatment of GC. Most of the researchers are guided only by their own long-term experience and the results of the leading world clinics dealing with this issue. Japanese researchers are the world leaders in studying this problem. The best treatment results were achieved in Japan since the adoption of the National Program for the Study of Gastric Cancer in the early 1960s. The Japanese Scientific Society for the Study of Gastric Cancer (JRS GC) and, later, the Japan Gastric Cancer Association (JGCA, 1998) have defined and described in details 16 groups of regional lymph nodes that form 3 consecutive stages of lymphatic metastasis of GC from various sections of the organ – N1-N3.

Stage 1: perigastric lymph nodes of the ligamentous apparatus of the stomach (Nos. 1-6);

Stage 2: lymph nodes along the branches of the celiac trunk (celiac trunk, left gastric artery, common hepatic artery, spleen gates and along the spleen artery, Nos. 7-11);

Stage 3: retroperitoneal lymph nodes of the hepatoduodenal ligament (No.12), the retropancreatoduodenal zone (No.13), along the upper mesenteric artery (No. 14), along the middle colonic artery (No. 15) and para-aortic lymph nodes (No. 16).

It should be noted that the lymph nodes can relate to different stages of metastasis depending on the localizations of the gastric tumour.

The involvement of N1-N2 reservoirs in the tumour process is considered as regional metastasis, whereas N3 serves for distant metastasis.

Table 1 - Different strategies of lymph node dissection

Type of intervention	Volume of lymph node dissection		
	N1	N2	N3
Standard gastrectomy D1	+	-	-
Standard radical gastrectomy D2	+	+	-
Extended radical gastrectomy D3	+	+	+

It should be immediately noted that this classification of radical operations is applicable only to some leading clinics of the world since in many cases D2-lymph node dissection is regarded as an extended one.

The first retrospective comparative analysis of the results of extended lymph node dissection was made by Mine et al. (1970). The authors showed some improvement in the results, especially in the detection of metastases in the lymph nodes; 5-year survival D0-1 and D2-3 totalled to 49%, 10% and 53%, 21%, respectively, in the presence and absence of metastases in the lymph nodes.

Kodama (1981) showed in a similar study an increase in 5-year survival from 33% to 58% when performing D0-1 and D2-3 lymph node dissection.

By 1990s, Japan has completed the methodology of extended lymph node dissection. According to prof. K. Maruyama (1995), one of the founders of the methodology, the expansion of surgery has increased the resectability of the process up to 95%, with a stably low mortality of 0.4%.

The analysis of treatment of more than 61,000 patients with GC in 98 institutions of Japan has shown that:

- at stage I without metastases in the lymph nodes, D2-3 lymph node dissection increases the survival rate up to 92.4% vs. 74% at D1-lymph node dissection;

- at stage II, standard and extended gastrectomy deliver a significant improvement in survival rate – up to 76.8% and 52.5%, respectively;

- at stage III, extended surgery provides a two-fold increase in survival vs. standard surgery – 45.7% and 24.6%, respectively.

D2-lymph node dissection is a standard procedure in Japan based on the accumulated experience of the leading clinics in terms of significant improvement in the long-term outcome with satisfactory rates of complications and mortality.

Despite the successes of Japanese researchers, European and American surgeons were only testing the technique of enlarged lymph dissection by the early 1990s. However, the sequence in the actions of Japanese researchers, the lack of reliable improvement in the results of various combined therapies have incentivized the study of efficiency of extended lymph node dissection in the surgical treatment of GC.

The German group for the study of gastric cancer is one of the leading schools in Europe. According to their classification,

the lymph node dissection D1 is a limited resection, while D2 is a complete or radical resection. More than 1.500 cases were analysed. The resection of more than 25 lymph nodes is the criterion for radical surgery. The German researchers consider the extended lymph node dissection to be most efficient at GC stages II and IIIa. With the prolapse of the tumour through all the layers of the stomach wall and massive lymphogenous metastasis, lymph node dissection does not improve the distant outcome.

At the II International Congress on Gastric Cancer (Munich, 1997), the Dutch group on the study of gastric cancer has presented the results of a randomized study of 711 cases of surgical treatment of GC (380 - standard surgery, and 331 - extended surgery). The authors came to a conclusion that the extended lymph node dissection did not provide a significant improvement in the long-term outcome of treatment (the 5-year survival rate of 60% and 55%, respectively) while the postoperative complications and mortality have doubled (25% and 43%, 4% and 10%, respectively).

Prof. Sasako (1999) has analysed the materials of the Dutch group randomized study and mentioned a good organization and a detailed statistical analysis of the material but emphasized that:

- The study included a large number of surgeons (multicentre study) with insufficient experience in performing such operations;

- The surgeons were not trained individually to perform extended lymph node dissection. Prof. Sasako believes that it could have increased the postoperative complications and mortality. One of the examples was the hardware suturing because the surgeon was not experienced enough to do manual suturing;

- Limited radicality of surgery for the same reason. According to the results, in the Dutch protocol the number of dissected lymph nodes was equal 13 at N1, and 11 at N2, while in the Japanese study, the figures were 35 and 25, respectively. Insufficient number of dissected lymph nodes increased the likelihood of early relapse and the retention of metastatic lymph nodes;

- Lack of standardization in surgery: splenectomy was not always conducted in similar cases what is a violation of the Japanese methodology of extended surgery;

In the future, at the III and IV International Cancer Congresses for gastric cancer the Dutch authors have confirmed the reliability of the analysis by Prof. Sasako. They noted the improvement of remote treatment results in the D2-lymph node dissection group and the presence of metastases at the stage N1, i.e. at the stages II and IIIa.

At the close of the IV Consensus Conference (New York, 2001) prof. M.F. Brennan noted that during the development of methodology of extended lymph node dissection in specialized centres the immediate results of surgical interventions were comparable, and the remote results were approaching the figures provided by JGCA. In view of the accumulated experience, D2-lymph node dissection is considered to be a sufficiently safe procedure and shall become an integral element of GC surgical treatment.

Experience of KazIOR in extended lymph node dissection. The thoracic centre of the Kazakh Institute of Oncology and Radiology (KazIOR) has analysed the direct outcome of surgical treatment of 348 patients (men – 208, and women – 140) with GC in 2011-2015. 268 (77.1%) patients had tumour process stage III. All the patients received extended gastrectomy: 292 – gastrointestinal gastrectomy, and 56 – gastrectomy through combined laparotomic access. 79.1% cases involved combined surgery as in most cases the spleen was removed in a single block with the stomach according to the developed methodology. The rationale for that was the need for monoblock removal of lymphatic reservoirs without separation of the ligament apparatus. In some cases, the caudal, or corpora-caudal, resection of the pancreas was made in order to preserve the elasticity and achieve the radicality of surgery.

The incidence of lymphogenous metastasis was 45.9% (152 cases). One of the most important results of lymph node dissection was a reliable staging of the tumour process which allowed assessing the efficiency of surgery. About 10% of patients migrate to a more advanced stage due to the metastases in the lymph nodes. The average number of removed lymph nodes was 24.3.

Postoperative complications were noted in 86 patients (24.2%), lethality - 15 patients (4.3%). The main reason for complications and mortality was the respiratory and heart failure.

The peculiarity of extended surgery is the development of such key aspects of surgical intervention as: monoblock removal of lymphatic reservoirs, safe treatment of pancreas stump during its resection, the formation of a reliable esophago-intestinal anastomosis and adequate drainage of the abdominal cavity. For example, the use of invagination bowl esophageal-small intestinal anastomosis of Gilyarovich in the modification of M.I. Davydov allowed reducing the probability of such a previously formidable and often fatal complication as an inconsistency of sutures of the oesophageal-intestinal anastomosis. On the other hand, the adequate drainage of

abdominal cavity with rubber-glove discharging drainages installed in the prognostically dangerous places (lien spleen, pancreas stump, etc.) also significantly reduced the number of ulcers of the abdominal cavity presented during the development of methodology.

Conclusions. The experience of extended surgery leads us to the following conclusions:

- GC is characterized by early lymphogenous metastasis;
- the reliable staging of tumour process is possible only during extended lymph node dissection on the basis of the staging of lymphogenous metastasis;
- Optimization of postoperative period allows reducing the number of complications and mortality in patients undergoing extended operations;
- lymph node dissection can reliably improve the long-term treatment outcomes and reduce the number of early loco-regional relapses.

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Psychological assistance to stoma patients. Psychological aspects of rehabilitation

The article discusses the specifics of providing psychological and rehabilitation assistance to stoma patients. Such assistance is influenced by many physical, social and psychological factors. They generate a complex of problems which cannot be solved without considering all components of health, disability, and functioning.

Keywords: oncology, psychology, stoma patients, rehabilitation.

Relevance. Psychological rehabilitation is one of the most important factors in returning of stoma patients to normal life.

Body integrity is one of the highest values existing at the sub-conscious level. Any surgical operation causes mental trauma to people which they realize and feel in different ways.

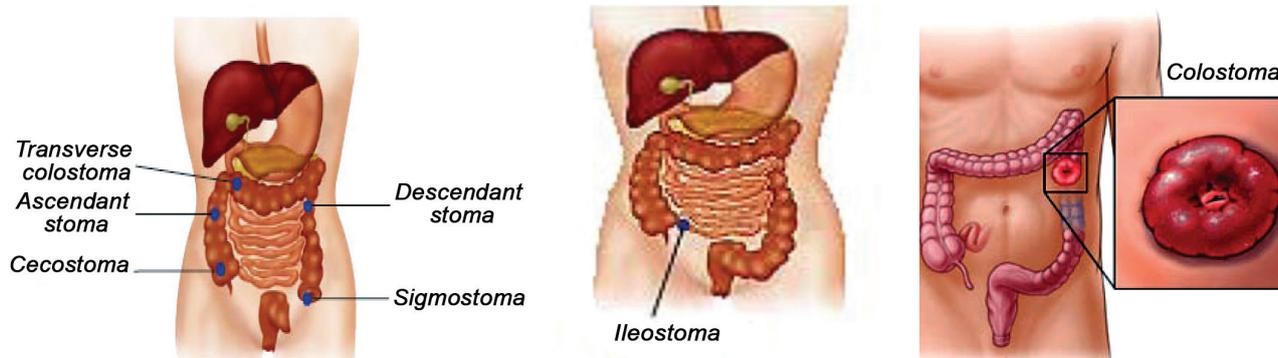
Introduction. The term «stoma» (ostomy, Greek) means a surgically created hole connecting the internal cavity with the surface of the body. There are different types of stoma, which are called by the organs to which they are imposed.

Stoma application is required when the intestine or bladder cannot function properly due to congenital defect, disease, or trauma.

The intestinal stoma is often called an «unnatural anus» since in this case the defecation goes not through the natural anus but through a hole formed on the anterior abdominal wall.

A stoma can be temporary or permanent. Temporary stoma can be applied if you cannot achieve good bowel preparation for surgery (when intestinal patency is impaired due to a tumor or adhesions). A temporary stoma might also be required to limit the passage of intestinal contents through the bowel – to avoid traumatization the place of surgical intervention by faecal masses. The intestinal function usually returns to the former level after the closure of a temporary stoma.

A permanent stoma cannot be removed in the course of further treatment of the patient if the obturative apparatus of the intestinal tract is absent or irreversibly damaged, or there is no possibility to promptly reconstruct the continuity of the intestine.



Psychological status of stoma patients. Most stoma patients experience emotional tension, concerns, anxiety, fear, feelings of despair and resentment in certain situations, as well as other psycho-traumatic feelings associated with:

- uncomfortable conditions during sleep, in sexual sphere, when visiting public places, and etc.;
- anxiety for their health in general;
- lack of experience in personal care for the stoma.

A few stoma patients can immediately return to their usual life. However, these manifestations disappear with a favourable resolution of the situation. First of all, in the postoperative period a stoma patient should learn that the number of stoma patients is quiet high and they can always seek help from the specialists in psychosocial care.

When a stoma patient returns home after surgery, he/she faces the problem of returning to the old style of life. If the person cannot solve this problem alone, he/she should request assistance from a psychologist.

A psychologist is a guide leading the patient's psyche on the way to peace. Forming a proper adequate attitude of a person to him/her-self means convincing him/her to:

- realize the mechanism of the disease and the changes that happened inside and outside, their nature;
- cope with the consequences of the surgery;
- cooperate with assistance specialists, especially at the initial stage of recovery.

Insufficient awareness of the patient and his fears are the main factors contributing to the emergence of psychogenic disorders.

The patient may be insufficiently informed about:

- the reasons for ostomy surgery;
- the extent of performed surgical intervention;
- the changes in the functioning of the body as a result of surgery;
- the possibilities to compensate the disordered functions of the body;
- the ways to obtain specialized medical and psychosocial assistance.

The patient may be concerned about the forced change in his family role and the need to change job or be registered as a disabled person.

As a consequence, more than 98% of stoma patients who did not receive sufficient information post-surgery fall into depression of varying degrees of severity: from light sleep disorders, mood lability, loss of appetite, etc. to a persistent rejection of their own body (being the main motivation for suicide).

Methods. The rational psychotherapy conducted before or early after surgery allows achieving a persistent positive attitude and acceptance by the patient of the fact of ostomy and, as consequence, an active participation of the patient in the process of rehabilitation.

The use of rational psychotherapy with stoma patients is extremely important.

The objectives of rational psychotherapy are: the realisation by the patient of psychological mechanisms of the disease, the reconstruction of disturbed relations of the patient as a person, the correction of inadequate reactions and forms of the patient's behaviour by affecting all the main components of a relationship - not only cognitive, but also emotional and behavioural, with the maximum participation of the patient in the process of treatment.

Preliminary understanding and interest of the patient in the forthcoming conversation with the psychologist are necessary prerequisites for using the method of rational psychotherapy.

Before the surgery, the patient should be informed about the possibility of imposing a stoma during the operation and the purpose of this manipulation. Such pre-surgery information and preparation are very important. They give confidence to the patient and make him/her aware of the possibility to return to normal life even with a stoma. It definitely refers only to planned surgery as at emergency operations, for example because of an acute intestinal obstruction, this stage of the rehabilitation process has to be neglected.

Psychological preparation of the patient is a very important and multifaceted process. The first thing a psychologist has to face is the painful concerns, sometimes, even the suspicion of the patient. It is partially caused by the fact that the psychologist is a new actor in the drama of the patient's illness. The patient has to receive the new information against the background of his/her concerns and suspicion;

and such information can cause ambiguous reactions: from tears to an emphatic refusal of surgery. That is why it is recommended to think over in details not only the necessary amount of information, but also the optimal form of its delivery. It is desirable to do it in a relaxed atmosphere, without unnecessary witnesses.

The psychologist should check with the attending physician the level of the patient's awareness, the diagnosis, as well as the scope and nature of the forthcoming surgery and, especially, the possibility for stoma application.

It is important to remember that life with a stoma is not disease. Modern means of stoma care allow such people to be fully functional in live, and even at work. But, as a new-born child, an operated person needs time to adjust to the changed conditions. And this is not only the problem of taking care of stoma, but also the moral perception of existence with a stoma.

Meanwhile, the stoma itself cannot destroy family relations if they've been strong before surgery. Namely the family, through a tactful approach, can help a stoma person return to usual life, fill his/her life with the former content and plans. Sexual relations only reinforce the relationship between the partners based on mutual respect, the desire to help each other, to share eventual problems. In the families that lack such relationship before surgeries, the stoma can become a formal reason for break up. The patient should be told that some manifestations of sexual dysfunction may be age-related and not directly related to the stoma surgery. In any case it should be emphasized that solving the sexual problems of a stoma patient requires special tact and understanding. There are no simple answers or solutions. However, the patient and his / her partner shall spend enough time to raise any possible questions about the changes in their sexual life.

Features of nutrition with a stoma. The disease and the surgery on the intestine that ended up with a stoma deprive the body of a lot of energy, vitamins, proteins, and minerals. This may result in the loss of body weight, increased fatigue, weakness, and feeling of oppression or irritability. Proper nutrition with a stoma will not solve all the problems but is a pre-requirement for a productive life.

NB: our patients and their relatives have a lot of questions regarding nutrition – there is a fear «to harm», fear of «relapse» because of possible malnutrition in the future.

To restore disordered bowel function, patients need to start making up their diet based on four main principles: regularity, cautiousness, graduality, and reasonableness.

Regularity is a very important principle. It allows the body to arrange production and release of food juices at the same time and therefore to improve the

process of digestion and absorption of nutrients and the release of the body from indigestible products. The more regular is the diet, the more regular is the intestine function; while uncontrolled nutrition will lead to the same uncontrolled operation of the stoma. It is necessary to develop a diet and strictly follow it, even in case of loss of appetite. People with colostomy with regular meals can achieve emptying of the intestine once a day, at the same time. The process of digestion much depends on conditioned reflexes that prepare the body to ingest and digest food. An apparently healthy person needs three or four meals a day; in calories, the breakfast should make 30% of the daily ration, the lunch – 40%, the afternoon tea – 10%, and the dinner – 20%.

Cautiousness is the principle for choosing of nutrition after surgery. For the time of formation of postoperative cicatrices (30-40 days), the diet should exclude products that cause gas formation: black bread, cabbage of any sort, egg in any form, onion and garlic, spices and condiments, grapes, mineral water with gases. Pickled, fatty and heavy foods shall be consumed with great caution.

Graduality is the principle of gradual introduction of new products in the diet not to cause an unpleasant reaction of the gut and the intestine. An eating log can help to determine within several weeks which products and in which quantities are more acceptable, and which should be avoided. The log shall contain records on the consumed products, their quantity and meal time, the time of defecation, the consistency of excretions, the odor and the amount of exhaust gases (by subjective sensations) through the stoma; as well as the occurrence of pains and the amount of urine.

Reasonableness - this principle is good in everything, including nutrition. The food shall be consumed frequently (up to 5 times a day) but in small portions.

Psychological rehabilitation. The presence of the stoma can oppress the patient's psyche causing transient asthenia. A warm atmosphere of understanding helps to return to the previous active life even a year after surgery. In persistent sexual dysfunction a person with stoma should visit a sexologist. The significant other should be the first to know about the stoma since his/her help and support ensure a quick rehabilitation.

The patient shall be explained that he/she does not have to constantly draw attention of the family members or relatives to the stoma and even more to show it. Still, the mystery around it can become a burden. This problem is quiet similar for single people with stoma. In any case, it is better to inform the partner about the stoma in advance, even if it leads to a break up. In the countries that have societies of people living with stoma («ASTOM» The regional public organization of disabled patients with stoma of the city of Moscow - www.astom.ru, the Public Association of Ostomy People of the Republic of Moldova - www.aops.webs.md), the patients might find their partners among the people with the same problems.

aops.webs.md), the patients might find their partners among the people with the same problems.

Each decision about informing the colleagues at work is taken individually. However, it should be taken into account that this can be negatively perceived by the management and the employees. Some people with stoma always conceal their stoma.

Criteria for the efficiency of psychological rehabilitation of stoma patients are:

- A complete psychological adaptation to the presence and functioning of the stoma;
- Full restoration of social status with the possibility to participate in social life without any limitations;
- Preservation of the family role;
- Restoration of work capacity to pre-surgery level, except for the heavy physical labour.

Positive changes in the way of thinking, the appearance, the attitude to life are the main indicators of mental and psychological recovery of the patient.

Recommendations to the relatives of stoma patients.

What to do when the patient is in the oppressed or depressive state?

The patient has become passive, has lost his/her will to live. Nothing pleases him/her. He/she has lost hope, and even talks about suicide. He/she keeps repeating that everything is bad. Of course, you want to argue that this is not so and the situation is not hopeless. Please note that he/she sees everything only in black colours. You will not succeed to distract him/her from problems. Do not say that everything is not as bad as it seems to be. Tell that you understand how hard and painful it is for him/her. Keep in mind that he/she is seriously thinking of suicide. Do not demand him/her to stop talking nonsense.

In fact, the patient does not want to commit suicide; he/she just needs understanding. This is the last way to draw attention to the hopeless situation, the way to find help and support. When a person feels that his/her situation is hopeless, he/she is afraid of unbearable pain, is afraid of becoming a burden for the others. And if he/she does not see any way out and feels that no one cares about him/her, he/she really may attempt a suicide. Watch for the patient, find out what he/she is thinking about. Be always near when it's hard for the patient. Let him/her feel your care. He/she needs consolation and needs to be heard. Do not stop the talks about suicide, talk to the patient about it. You can also take a promise that when such thoughts come again he/she will call you and wait for you. Never say: «You will overcome this», «Be patient, «Everything will be good» because the patient realizes that nothing will be good for him/her. He/she will only feel that you do not understand him/her and will hide his/her thoughts from you. Do not demonstrate your superiority, do not say: «What stuff!» as all the patient is talking about is important for him/her. Channel his/her thoughts in

another direction. Make him/her do something to have less time to think about the bad.

What to do when the patient shows hostility?

Caring for a hostile person can easily cause stress. Such person will always be dissatisfied with what you do no matter how hard you try.

Remember that his/her irritation is caused by discontent with him/her-self and the situation as a whole, and, in fact, is not related to you. Outbreaks of hostility are normal reaction to stress but they make communication difficult. Hostility can manifest itself indirectly. If a person does not like something, he/she might say nothing directly but can become gloomy, start blaming you and refusing your help, stop following the instructions and do everything to spite.

You should not start avoiding the patient. Even when he/she refuses help and repels the relatives, he/she needs them. You should understand that the hostility is a manifestation of helplessness and is caused by high inner tension. In this condition, the abilities for communication and logical thinking are limited, the perception and understanding are egocentric. Your impatient and irritated attitude to a hostile patient might only intensify his/her antipathy and irritation.

Communication. The person with stoma needs to be listened to and needs to give vent to his/her hostility. You should neither exert moral pressure, nor agree with everything. Stay calm, give clear instructions. Keep going until the patient calms down. Try to avoid confrontation. Take care of satisfying his/her physical and emotional needs. Hostility can be caused by unmet needs. Moreover, the ward does not always realize it. Keep in mind that an emotional person does not always hear the details and does not always fully understand the essence of what is said. If you are affected by feelings you always lose objectivity. **To keep the situation under control:**

- Try to listen to the ward;
- Do not start to immediately defend yourself and appeal to his/her conscience;
- Ask him/her what's wrong and why he/she accuses you;
- Find out what the problem is.

In most cases, the reason for hostility is not you, but something else. As a rule, the reason is epy helplessness and depression of the patient. Give him/her the opportunity to describe what the cause of hostility is. Ask again and specify what he says, so that he/she does not just blame you, but outlines the facts and expresses his/her needs. If the patient says that no one cares about him/her, ask about his/her wishes and the idea how the care should look like. If you show your concern, you can establish the contact, and the patient will calm down.

Remember that you need to control your feelings because hostility breeds reciprocal hostility. And only your smooth calm attitude can extinguish it.

To take a hold on yourself:

- Control yourself and your thoughts;
- Control your gestures, they must be slow and smooth;
- Speak in a pleasant and confident voice.

Your reaction can cause the ward to calm down or confront; it can weaken or strengthen the hostility of the ward. If you stay calm, let the ward speak out and «let off steam» he/she might be able to listen to you too. If you have any requirements to the ward, state your point of view with calm confidence and do not back off from it.

You may even need to seek help from a psychiatrist because antidepressant medications may be required with a severe form of depression.

Let the ward take care of him/her-self as much as possible. When the patient wishes to take care of oneself it's a big step forward. Think of something that your ward could control by him/her-self. At a situation of choice, a person has a better control over its life. The best way to ease the negative emotions is to provide a moderate physical load, such as walking, gymnastics, games. Use the means of relaxation – massage, water treatment, etc. Remember that the ward will need some time to recover and have the will to live.

Life goes on – that's the main thing the person with stoma shall remember and use as the grounds for further recovery. He/she should never cut off from the world, go into shell, avoid contacts with people.

It is very important to organize «Schools for patients» at the hospitals and clinics to inform the patients with stoma about:

- how the stoma functions;
- how to use stoma care items;
- how to eat properly and, if possible, keep a rut;
- who to contact for medical matters, if necessary.

Conclusions. Multi-level rehabilitation is required taking into account the complexity, specificity and variety of the problems of reintegration of individuals with anatomical impairments of the excretory function in the form a stoma of intestines or ureters. An integrated concept of the phenomenon of health and its disorders shall be recognized.

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The role of X-ray examination in gastric cancer diagnostics

X-ray examination methods are an accessible, relatively inexpensive method of early detection of gastric cancer (GC). 1038 patients aged 12 to 92 years underwent X-ray examination of the stomach at the Kazakh Institute of Oncology and Radiology. The article presents the results of diagnostic use of X-ray examination methods.

Keywords: radiography, radioscopy, gastric cancer.

Relevance of the study. Worldwide indicators show a certain downward trend in the incidence of gastric cancer (GC): currently it ranks fourth (8.4%) in the global pattern of morbidity. However, the mortality remains high (10.4%), and GC is the second cause of death after lung cancer. One of the reasons for low survival rate is the late detection of GC [2, 3].

In the oncology pattern of the Republic of Kazakhstan, GC ranks fourth in morbidity (16.3%), and second in mortality. 2736 new cases were recorded in 2012. Of them, only 27.1% were diagnosed at an early stage, and 27.4% - at the late stages [1]. X-ray method remains one of the main methods of GC diagnostics [4].

Material and methods. 1038 (100%) patients of the X-Ray Diagnostics Department of KazIOR underwent X-ray examination of stomach and duodenum from 01.01.2015 till 01.11.2016. The treatment arm included 182 (18.0%) patients (average age – 60.4 years) diagnosed with GC by clinical and X-ray methods. The control arm included 721 patients (69.0%) with other established diseases of the gastrointestinal tract. 135 (13.0%) patients previously diagnosed with GC underwent a repeated X-ray examination, and therefore were excluded from this study.

X-ray examinations of the stomach followed a standard procedure with barium sulphate using Philips DuoDiagnost apparatus with multiple view radioscopy and radiography. X-ray examination of the stomach included three steps: 1) the study of the relief of stomach folds; 2) double contrasting of the stomach; and 3) tight filling of the stomach.

Results. Distribution of the patients by sex: The patients' distribution by sex is shown in Figure 1.

As can be seen in Figure 1, the treatment arm included 37.4% of women, and 62.6% of men vs. 55.6% of women and 44, 4% of men in the control arm. Thus, the treatment group had more GC cases in men, and the control arm – in women. In total, GC was 1.7 times more frequent in men than in women.

Distribution of the patients by age: The patient's distribution by age in the treatment and control arm was as follows (Figure 2).

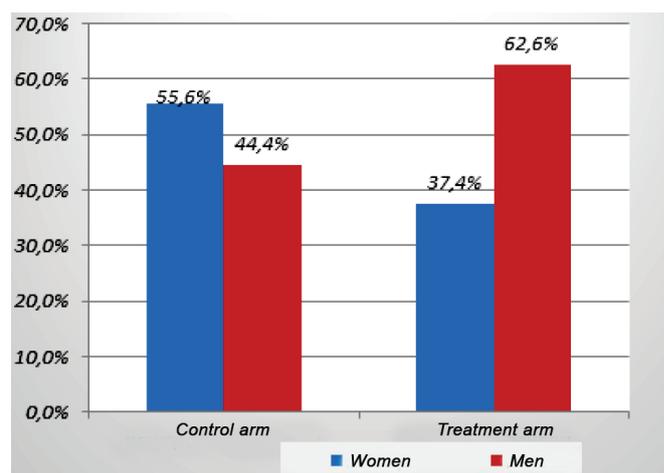


Figure 1 - Distribution of patients by sex in the treatment and control arms

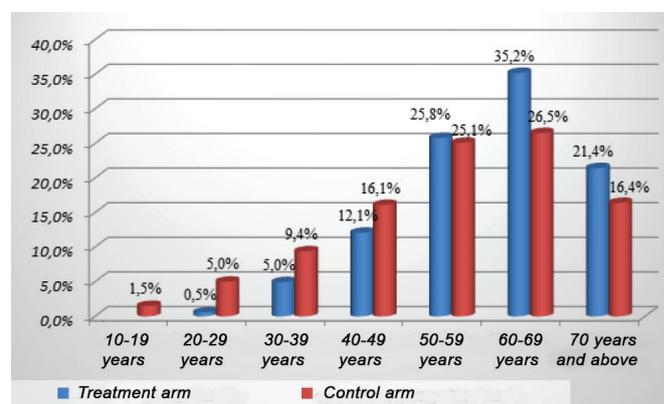


Figure 2 – Distribution of patients by age in the treatment and control arms

According to Figure 2, most of the patients (35.2%) newly diagnosed with GC were 60 to 69 years old, 25.8% of them were 50 to 59 years old what is 9.4% less, 21.4% of them were 70 years old and above, 40 to 49 y.o. – 12.1%, 30-39 y.o. – 5.0%, and 20-29 y.o. – only 0.5% of cases. In the control arm, most of the cases related to patients aged 60 to 69 (26.5%) and 50 to 59 (25.1%), a bit less – to patients aged 70 and over (16.4%) and 40 to 49 (16.1%) years. GC was rare at the age of 30-39 (9.4%), 20-29 years (5.0%) and 10-19 years (1.5%). Thus, the majority of GC cases in the treatment group related to the age of 60-69 years (35.2%) while in the control arm most of the cases fall into the age group of 50 to 69 years.

Distribution of patients by the form of growth of the neoplasm: We also analysed the results of X-ray examination in the treatment arm by the form of growth of GC. The forms were divided into three groups: endophytic, exophytic, and mixed (Figure 3).

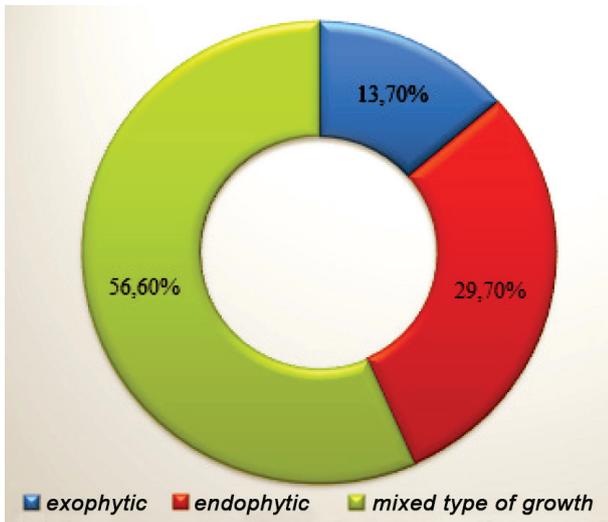


Figure 3 - Distribution of gastric cancer (GC) by the form of growth

Figure 3 above shows the distribution of GC by the form of growth: the mixed type of growth prevailed (56.6%) followed by endophytic (29.7%) and exophytic (13.7%) types of growth.

Distribution of patients by localization of the process: Next, we analysed the distribution of GC patients by localization of the process.

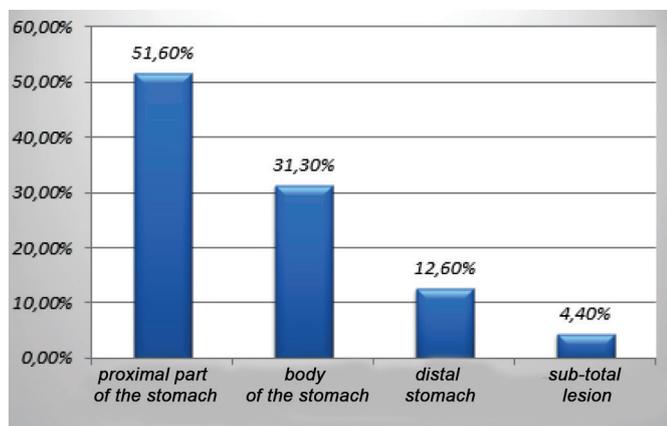


Figure 4 – Distribution of patients with gastric cancer (GC) by the localization of the process.

According to the X-ray examinations (Figure 4), the GC most often affected the proximal part of the stomach (51.6%) and the body of the stomach (31.3%), less often it was localized in the distal stomach (12, 6%). Subtotal lesion of the stomach was observed in 4.4% of cases.

X-ray symptoms of GC. We also studied the incidence of X-ray symptoms of GC. Figure 5 shows that the most common symptoms of GC included: the change in the relief (rupture of the mucosal folds) – in 92.3%, and the aperistaltic area – in 91.3% of cases while in the control arm the change in the relief (pathological restructuring) was observed only in 9.7%, and the aperistaltic region -

in 2.4% of cases. The filling defect in the treatment arm was observed in 54.9%, and the stomach deformation – in 28.0% of cases while in the control arm the filling defect was observed only in 10.4%, and the stomach deformation – in 14.3% of cases.

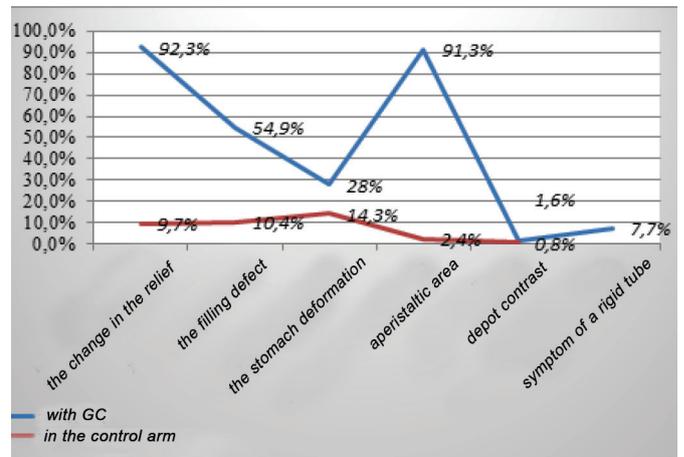


Figure 5 – Distribution of X-ray symptoms at gastric cancer and in the control arm

The radiological symptom, barium depot, was found in 1.6% of cases in the treatment arm, and in 0.8% of cases in the control arm. The symptom of a rigid tube was found in 7.7% of patients with GC vs. zero cases in the control arm. Thus, the rupture of folds and the presence of aperistaltic area can be considered as reliable pathognomonic symptoms of GC.

The histological type of GC growth was studied in 79 patients with GC. Most of the tumours were adenocarcinomas (68.3%), of them: low-differentiated – 35.4%, moderately differentiated – 27.9%, and highly differentiated – 5.0%. Gelatinous carcinoma and undifferentiated GC were equally common and observed in 13.9% of cases; adenosquamous gastric carcinoma was less frequent – 1.2% of cases.

Conclusions. In the study, men had GC 1.7 times more often than women. The highest GC incidence was observed at the age of 60-69 (35.2%). The mixed type of growth (56.6%) prevailed. According to the X-ray, the proximal part of the stomach was most often affected (51.6%). The rupture of the mucosal folds (92.3% of cases) and the presence of aperistaltic area (91.3% of cases) can be considered as pathognomonic symptoms of GC.

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PANCREATIC CANCER

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The influence of polymorbidity on the results of treatment of patients with gastric cancer and pancreatic cancer

We made retrospective analysis of records of patients with gastric cancer (19 patients) and pancreatic cancer (36 patients) treated in the National Center of Oncology in 2012. The identified polymorbidity has influenced the malignant process and the treatment outcomes.

Keywords: polymorbidity, gastric cancer, pancreatic cancer.

Relevance. Polymorbidity (the presence of multiple clinical nosologies in one patient) is a serious problem in the clinical practice of today not only due to the growing number of such patients and the challenges in their diagnostics and treatment, but also due to the severe condition of such patients, the «masking» effect of different nosologies, the similarity of syndromes, and the worsening of treatment prognosis. Polymorbidity means the involvement of various physiological systems in the pathological process. Modern medicine reasonably considers a certain non-specific generality in the mechanisms of pathogenesis of the most common pathological processes [1].

The clinical picture of the underlying cancer disease might be distorted by the presence of a number of comorbidities like hypertension, diabetes, coronary heart disease, renal pathology, and bronchopulmonary pathology [2].

Polymorbidity is not just a statement of the fact that the patient has several diseases; it is an additional death risk factor. Formed polymorbidity in patients has its own independent nature and is a new pathophysiological condition [3, 4].

Currently, endothelial dysfunction and the associated deficit of nitric oxide, high activity of free radicals lead to a massive production of cytokines (the so-called «cytokine storm») which damage the mitochondrial membranes and then – the cell membranes being the key factor in the development and increase of the disease severity in polymorbid patients [3, 4].

Purpose of the research – to study co-morbidities in cancer patients and their effect on the treatment course and outcome.

Material and methods. We conducted a retrospective analysis of case histories of patients with gastric cancer (19 patients) and pancreatic cancer (36 patients) treated at the National Cancer Center in 2012.

Due to the difficulty of biopsy even during surgery, the histological verification was available only for two patients. In other cases, the pancreatic cancer was diagnosed based on the clinical data, the results of ultrasound and computer tomography examinations.

The polymorbidity in patients definitely affects the course of the malignant process and the treatment outcome.

The statistical processing of data was made by the method of assessing the significance of the differences between two data sets by applying the t-Student criterion. Ranking of statistical phenomena was made using factor analysis and F (Fisher) criterion. «STATGRAPHICS plus for Windows» [5] software was used for mathematical and statistical processing of data.

The diagnosis was morphologically verified in all the patients. The majority of the patients had low-differentiated adenocarcinoma (47.3%). All the patients had advanced cancer.

Group I included the patients with pancreatic cancer (36 people), of them, men – 24 (66.7%), women – 12 (33.3%), aged 43 to 84 (average age – 56.7 ± 1.2) years old.

As the age of patients influences their comorbidities, the patients were conditionally divided into 2 subgroups: 34 to 60 years (24 patients, 66.6%) and over 60 years (12 patients, 33.3%).

Group II included the patients with gastric cancer (19 people), of them, men – 14 (73.7%), women – 5 (26.3%) (average age – 61.0 ± 2.2 years old).

For the study of comorbidities, Group II was also conditionally divided into two subgroups: 34 to 60 years – 10 patients (52.6%), and over 60 years – 9 patients (47.4%).

Results and discussion. Studying the aspects of comorbidities in patients of different ages with gastric and pancreatic cancer, we found a certain pattern of polymorbidity related to a certain localization of the malignant process. Thus, the patients with pancreatic cancer stages III and IV had hypertension, pyelonephritis, coronary disease, diabetes mellitus; while the gastric cancer was mostly associated with the coronary disease, the liver pathology (in the form of cholelithiasis), and hypertension.

Tables 1 and 2 provide data on age-related comorbidities in patients with pancreatic and gastric cancer.

Table 1 – Associated comorbidities in patients with pancreatic cancer

Comorbidities	Middle age patients (40-60 years), n = 24			Aged patients (over 60 years), n = 12			P
	No. of patients, n	%	factor weight	No. of patients, n	%	factor weight	
Concomitant hypertension	13	54,2	0,92	6	50	0,84	> 0,05
Coronary disease	20	83,3	0,95	10	83,3	0,96	> 0,05
Obesity	9	37,5	0,66	4	33,3	0,58	> 0,05
Liver pathology	15	62,5	0,82	11	91,7	1,6	< 0,001
Diabetes mellitus	9	37,5	0,72	5	41,6	0,79	> 0,05
Pyelonephritis	15	62,5	0,83	10	83,3	1,5	< 0,001
Prostatic hyperplasia	6	25	0,56	10	83,3	1,46	< 0,001

Table 2 - Factors associated with polymorbidity in patients with gastric cancer

Comorbidities	Middle age patients (40-60 years), n = 24			Aged patients (over 60 years), n = 12			P
	No. of patients, n	%	factor weight	No. of patients, n	%	factor weight	
Concomitant hypertension	13	54,2	0,92	6	50	0,84	> 0,05
Coronary disease	20	83,3	0,95	10	83,3	0,96	> 0,05
Obesity	9	37,5	0,66	4	33,3	0,58	> 0,05
Liver pathology	15	62,5	0,82	11	91,7	1,6	< 0,001
Diabetes mellitus	9	37,5	0,72	5	41,6	0,79	> 0,05
Pyelonephritis	15	62,5	0,83	10	83,3	1,5	< 0,001
Prostatic hyperplasia	6	25	0,56	10	83,3	1,46	< 0,001

As obvious from Table 1, middle age patients had significantly less liver changes in the form of increased bilirubin and transaminase vs. the aged group. This is associated with obturation of bile passages by the tumour and is much more manifested in aged patients what evidences the more advanced process in this category of patients. The patients above 60 years had more frequent cases of pyelonephritis and prostatic hyperplasia.

No patients underwent radical treatment, still 16 (66.6%) of the middle age patients underwent surgical enterocholecystostomy, and 8 (33.3%) received symptomatic treatment. In the elder group, only 4 patients got anastomosis (33.3%), the remaining 8 patients did not receive surgical treatment because of their severe condition (66.7%).

In the group of patients aged 40 to 60 years, 8 patients (80%) underwent surgical treatment and chemotherapy, and only 2 patients received symptomatic treatment. In the group of patients above 60 years, 4 (44.4%) patients underwent surgical treatment, and the rest 63.6% received only symptomatic treatment.

As can be seen from Table 2, aged patients had more cases of past AMI, bronchopulmonary pathology, coronary disease, and cholelithiasis. This pathology affects the course of the disease, shades the clinical picture of the cancer process and influences the choice of radical treatment of cancer patients.

Conclusions. We came to the conclusion that polymorbidity was manifested by various co-morbidities at different cancer localizations. Pancreatic cancer was mostly associated with pyelonephritis, diabetes mellitus, arterial hypertension, and coronary disease while the majority of patients with gastric cancer had cholelithiasis, AMI, coronary disease, or bronchopulmo-

nary pathology. All that served as an unfavorable factor in the choice of treatment of cancer patients.

Modern medical practice dictates the need for an integrated approach to the study of the clinical picture of the onset and development of comorbidities necessitating a new look at the problem of polymorbidity.

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Correction of endothelial dysfunction in patients with pancreatic head cancer and its clinical outcome

95 operated patients with cancer of the head of the pancreas of clinical stages II and III were examined to analyse the changes in endothelial function after surgery against correction. Function indicators of endothelium and circulating endothelial content were tested.

The use of L-arginine and ACE inhibitor in complex treatment decreased the endothelium damage and supported the correction of endothelial dysfunction. The developed methods of treatment were also associated with fewer complications.

Keywords: pancreatic head cancer; endothelial dysfunction; L-arginine; inhibitor of the angiotensin-converting enzyme.

Introduction. The general state of the body plays an important role in determining the outcome of surgical and conservative treatment of malignant neoplasms [1-3]. This condition is determined by the presence or absence of disorders of system and regional hemodynamics, breathing, functioning of the indicators of biochemical systems, production and utilization of hormones, and etc. [4, 5]. A universal aspect in this case is the functioning of vascular endothelium depending on its morphology, also in the tumour.

Microenvironment of endothelium in tumour tissue, chronic hypoxia of endotheliocytes, frequent vascular injury determine the formation of system mechanisms aimed at activation of vascular-platelet haemostasis, vasoconstriction, the production of growth factors and inflammatory cytokines [6].

Growth of the pancreatic cancer head is usually associated with severe metabolic disturbances, the intoxication syndrome, malabsorption and maldigestion that worsen the overall condition of the patients and increase the risk of negative treatment outcome [7]. Under these conditions, the improvement of systemic parameters of blood circulation can significantly improve the surgical treatment outcome.

Purpose of the study: analysis of changes in endothelial function in patients with pancreatic head cancer after surgery against a background of correction.

Materials and methods. 95 patients with Stage II (T3N0M0 (2a), T1-3N1M0 (2b)) and Stage III

(T4N1M0) pancreatic head cancer (45 and 50 patients, respectively), of them, 66 men and 29 women aged 40 to 65 (mean age 60.8 ± 2.1 years) were examined. All patients underwent combined therapy including radical surgical treatment in the form of gastro-pancreatoduodenectomy or pancreatoduodenectomy.

Patients with severe comorbidities were excluded from the study. An obligatory criterion for inclusion was the informed consent of patients for the administration of additional methods of conservative treatment and the anonymous use of the findings in the scientific study.

All patients were divided into two groups by the use of additional perioperative therapy aimed at the correction of endothelial dysfunction. The patients in different groups had no significant discrepancies in terms of age, sex, stage of neoplasm, tumour localization in the stomach, the severity of condition in preoperative period, the concomitant diseases and the conducted surgical interventions.

The control arm included 40 practically healthy individuals aged 40 to 65 (mean age 57.3 ± 2.0 years).

The studied indices of vascular endothelial function included: the content of desquamated (circulating) endotheliocytes in the blood (CE), the von Willebrand factor (vWF) in plasma and the degree of endothelium-dependent vasodilation (EDVD) [8].

Clinical results were reviewed to detect purulent-septic, thrombotic complications early postoperatively and prospectively (2.1 ± 0.1 years in the treatment arm and 2.0 ± 0.2 years in the comparison arm).

Additional therapy aimed at the correction of endothelial dysfunction included L-arginine (vasoton, Barnaul, R.F.) 1.0 g 1/1 with ACE inhibitor (enalapril) 5 mg 1/1. The therapy started 3-4 days pre-surgery. Contraindication for ACE inhibitor was the expressed arterial hypotension (systolic pressure below 90 mmHg). Patients with such hemodynamics were excluded from the study.

The statistical significance of differences in indicators in groups and in dynamics was estimated by Mann-Whitney using the bootstrap method [9].

Results. The top line findings of the analysis of indicators in patients with pancreas head cancer are presented in Figures 1-3.

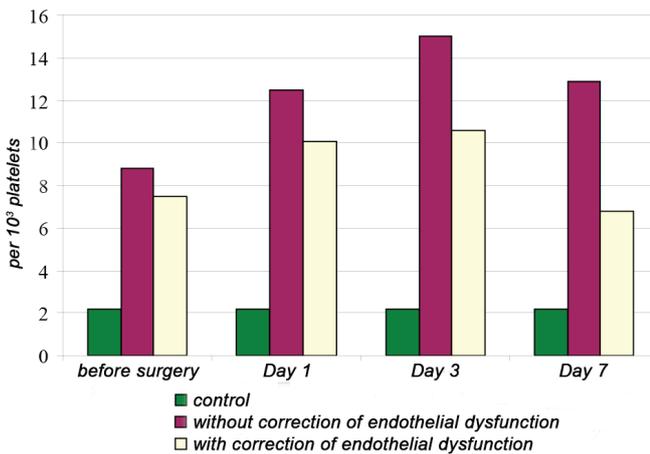


Figure 1 – Comparative analysis of the median content of circulating endotheliocytes in patients with pancreatic head cancer

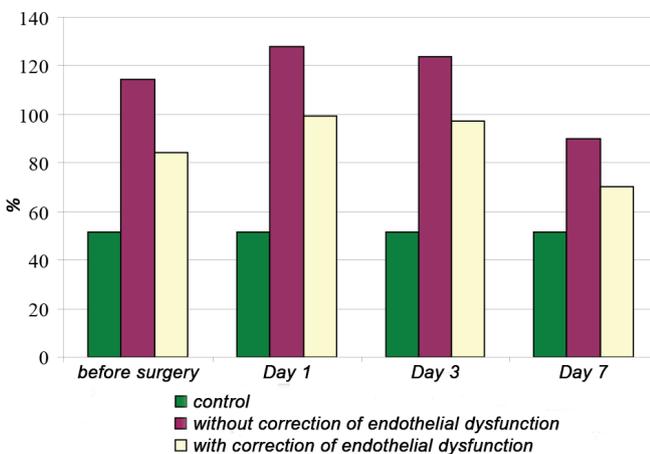


Figure 2 – Comparative analysis of the median value of von Willebrand factor in patients with pancreatic head cancer

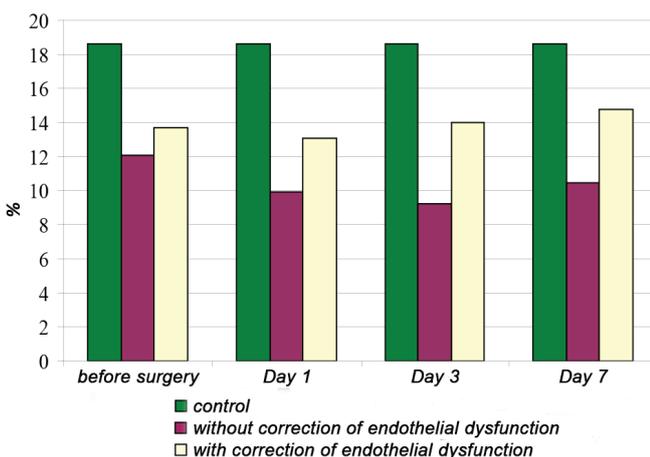


Figure 3 – Comparative analysis of the median value of von Willebrand factor in patients with pancreatic head cancer

There were some statistically significant deviations in vascular endothelial parameters from the values in the control arm both before and after the surgery in dynamics. The CE value sharply exceeded the control values at the outcome (Me/Me = 3.41), with the highest values on Day 3 after

surgery (Me/Me = 4.82), and a decrease on Day 7 (Me/Me = 3.09, $p < 0.01$ in all cases).

The groups of patients with pancreatic head cancer selected depending on the treatment differed in the CE value from Day 1 after surgery. The differences were statistically significant (Me/Me = 1.28, $p < 0.05$) and have increased on Day 3 (Me/Me = 1.56, $p < 0.05$) and Day 7 (Me/Me = 1.91, $p < 0.01$). As in the previous group, we detected the protective effect of conservative treatment performed before surgery on the level of damage to the vascular endothelium.

This is proven by the analysis of von Willebrand factor (vWF) in blood. Before the surgery, that indicator was relatively higher vs. control arm (Me/Me = 1.63), with the highest value on Day 1 (Me/Me = 1.92), and the same downward trend afterwards. On day 7, the difference with the control arm was 1.36 times ($p < 0.05$ in all cases).

On Day 1 after surgery, the vWF content in the comparison arm was higher compared to the treatment arm (Me/Me = 1.21, $p < 0.05$). On Day 3, the difference remained at the same level (Me/Me = 1.28, $p < 0.05$); on Day 7 it increased up to Me/Me = 1.54 ($p < 0.05$) due to more rapid dynamics of compensation in the treatment arm.

The EDVD level in the comparison arm was decreasing after surgery. In the treatment arm, on the contrary, the differences of the values with the control arm on Day 7 days were less than at the outbreak of the study. The most significant differences in that indicator were registered on Day 1 after surgery (RR = 1.42, $p < 0.05$).

At the outcome, there were no statistically significant differences between the arms. The difference increased one day after surgery (Me/Me = 1.36, $p < 0.05$). On Day 3, the differences between the arms reached the maximum level of RR = 1.55 ($p < 0.05$). On Day 7 the difference between the groups of patients with pancreatic head cancer has decreased, but was still statistically significant (Me/Me = 1.42, $p < 0.05$).

Table 1 presents the clinical results of treatment of patients depending on the received therapy.

The differences in the relative rates of complications in the early postoperative period were relatively moderate, but still statistically significant (RR = 1.75, $p < 0.05$ for Stage II, and RR = 1.70, $p < 0.05$ – for Stage III of pancreatic head cancer).

In contrast, 2 years of prospective follow-up revealed very significant differences in the incidence of relapse and metastasis: for the clinical stage II – up to RR = 2.63, $p < 0.05$, and for the clinical stage III – RR = 2.34, $p < 0.05$. The low level of statistical significance was associated with a small number of complications in the treatment arm.

Table 1 - Treatment outcome of patients with pancreatic head cancer

Indicator	Patient arms				P
	Treatment arm (n = 44)		Comparison arm (n = 51)		
	abs. number	%	abs. number	%	
Presence of complications in early postoperative period	10	22,7	20	39,2	>0,05
Presence of relapses and / or metastases	7	15,9	20	39,2	<0,05

Conclusion. The patients with pancreatic head cancer involved in the study had significant dysfunction of the vascular endothelium manifested by the increase in the content of circulating endotheliocytes which evidences the damage to the endothelium [10] and the reduction in vasodilating and anti-aggregatory properties. These changes were clinically proven. Expressed endothelial dysfunction led to a significant increase in the number of complications in the early postoperative period.

The use of additional therapy with the combination of L-arginine and an ACE inhibitor aimed at the correction of endothelial dysfunction contributed to a reduction in the number of complications what should be associated with the correction of endothelial dysfunction. Patients in the treatment group had less damage to the endothelium what was confirmed by a significant decrease in the number of circulating endotheliocytes, the content of pro-aggregate von Willebrand factor, and the increase in the endothelium-dependent vasodilatation index.

These changes could promote the improvement of condition of microcirculatory bed in the area of anastomosis and, moreover, the permeability of the blood channel at the level of arteries of medium diameter. It also corresponds to the results obtained by other authors [11, 12].

In general, the obtained results testify to the possibility of using the developed method of treatment in a complex of perioperative management of patients with pancreatic head cancer as well as with other neoplasms of the gastrointestinal tract.

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RECTAL CANCER

UDC: 616.351-006.6-036.22

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**Rectal cancer incidence trends
in Northern and Central Kazakhstan**

The article illustrates the rectal cancer incidence in Northern Kazakhstan in 2000-2009. 3,185 new cases of colorectal cancer were reported, accounting for 4.3% of the total cancer incidence structure. Age-standardized cancer incidence in the region equalled to 8.62 per 100,000 of population.

Keywords: rectal cancer, incidence, age-specific indicator.

Relevance. Rectal cancer (RC) is an acute problem of oncology because its incidence and mortality are growing each year [1, 6]. The International Agency for Research on Cancer (IARC) reports around 1 million 200 thousand cases of colon cancer worldwide, almost 30-50% of them being colorectal cancer [7]. A common mechanism of development of rectal cancer and colon cancer result in an identical strategy for their treatment and prevention [1, 3]. In most of the developed countries, colorectal cancer ranks 6-8th in the structure of cancer morbidity. The most complete epidemiological studies were conducted in highly developed countries of US, Canada, Australia, Northern and Western Europe with high morbidity rates of 30-40 per 100,000 [4, 5]. For most Asian countries, incidence rates do not exceed 15-20 per 100,000. Nevertheless, according to recent data, these countries also have an increase in the incidence of colon cancer [2].

Purpose of the study was to study the geographical variability of RC in Kazakhstan.

Material and methods. Northern part of Kazakhstan hosts 4 regions – Akmola, Qostanay, Karaganda, and North Kazakhstan regions and the city of Astana.

The study period is 2000 to 2009. The material included all cases of RC registered by the specialized and non-specialized medical institutions of Kazakhstan, as well as by the Civil Status Registration Offices. To avoid duplication, the data was alphabetized and grouped according to the International Classification of Diseases (ICD-10). As the descriptive epidemiology mainly studies the dimensional and temporal changes in the incidence of malignancies, we have calculated directly or indirectly the standardized incidence rates for RC. Methods of graphical and dimensional analysis, the studies on mapping the frequency of RC were utilized. Each registered case of RC was accompanied with the data on the general and sex population of the relevant region. The data on the adult population in the age

groups (0-29, 30-39 ... 70 and above) was also used. Each registered case of RC was accomplished by the type of medical institution where the RC was primarily diagnosed. The peculiarities in the distribution of the CR were revealed by comparative study of the relevant indicators of the incidence. Age-specific incidence indicators are calculated. Standardized incidence rates were determined by direct standardization of incidence rates using the world standard population.

Results.**RC epidemiology in Akmola Region.**

In the mentioned period, 701 patients with RC were registered in Akmola region to make 4% in the structure of malignant tumours. The intensive incidence was growing with the age. The incidence in the target group of 0-29 years varied from 0.1 to 0.2 per 100,000 vs. 1.3 (both sexes) at the age of 30-39, and 6.0 for men and 7.0 for women at the age of 40-49. At the age of 50-59, the incidence among men (18.2) was higher that among women (14.6).

The first peak of high incidence of this localization in the region (58.5) was registered among men of 60-69 years old (Figure 1).

The second peak of high incidence was also registered among men at the age of 70 years and above (86.0), while among women the indicator was equal to 41.1.

The intensive rates of RC morbidity in the region tended to increase from 10.1 (2000) to 11.1 (2003), followed by a decrease to 9.5 (2007) and 9.21 (2009) ($T_{in} = 0.00\%$) (see Figure 2). Standardized indicators decreased from 9.3 to 8.0 ($T_{st} = 0.03\%$). According to that data, the age structure of the population in Akmola region did not meet the world population standard.

The intensive RC incidence rate has increased among men from 8.6 at the beginning of the period to 13.5 in 2008, followed by a decrease up to 10.4. The rates of intensive ($T_{in} = 0.3$) and standardized ($T_{st} = 0.3$) incidence coincided. Among women, those indicators tended to increase from 8.6 (2000) to 12.6 (2008), with a subsequent decrease to 10.4 in 2009. The share of RC by age group was growing unimodally with the peak at the age of 60-69 (37.1%).

Thus, the annual intensive incidence of RC was equal to 9.3 ± 0.4 , with the standardized incidence of 8.1 ± 0.4 per 100,000.

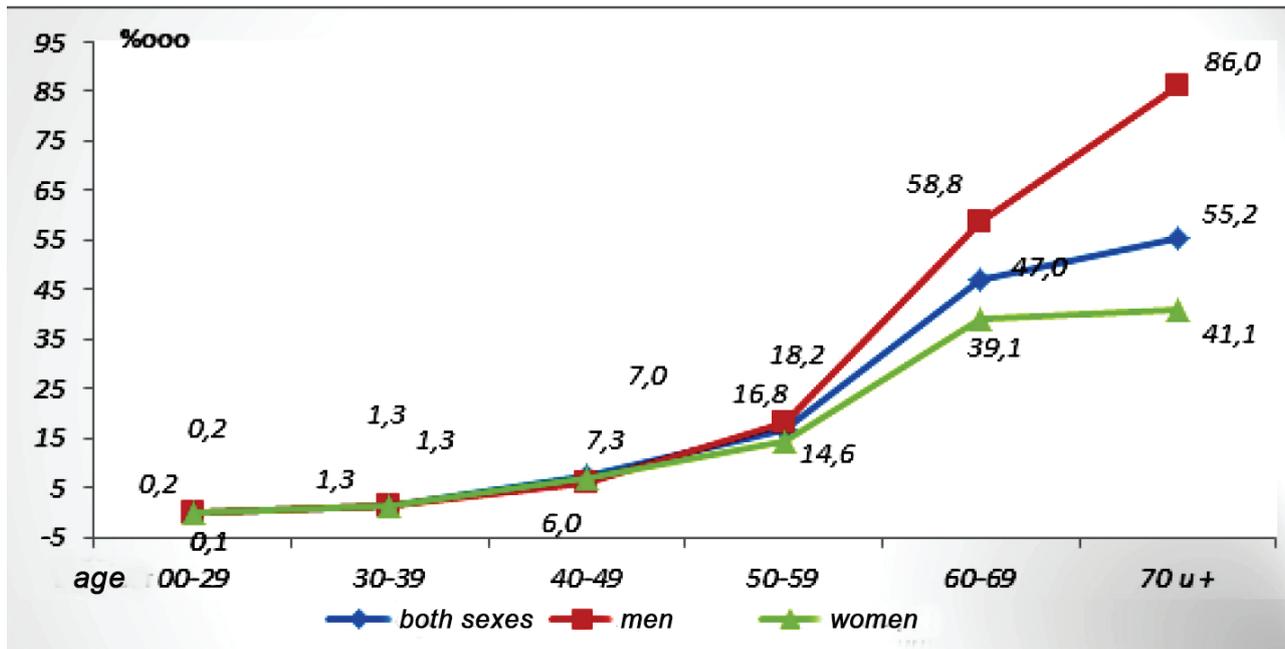


Figure 1 - Average annual sex- and age-related intensive incidence indicators of rectal cancer (RC) in Akmola region.

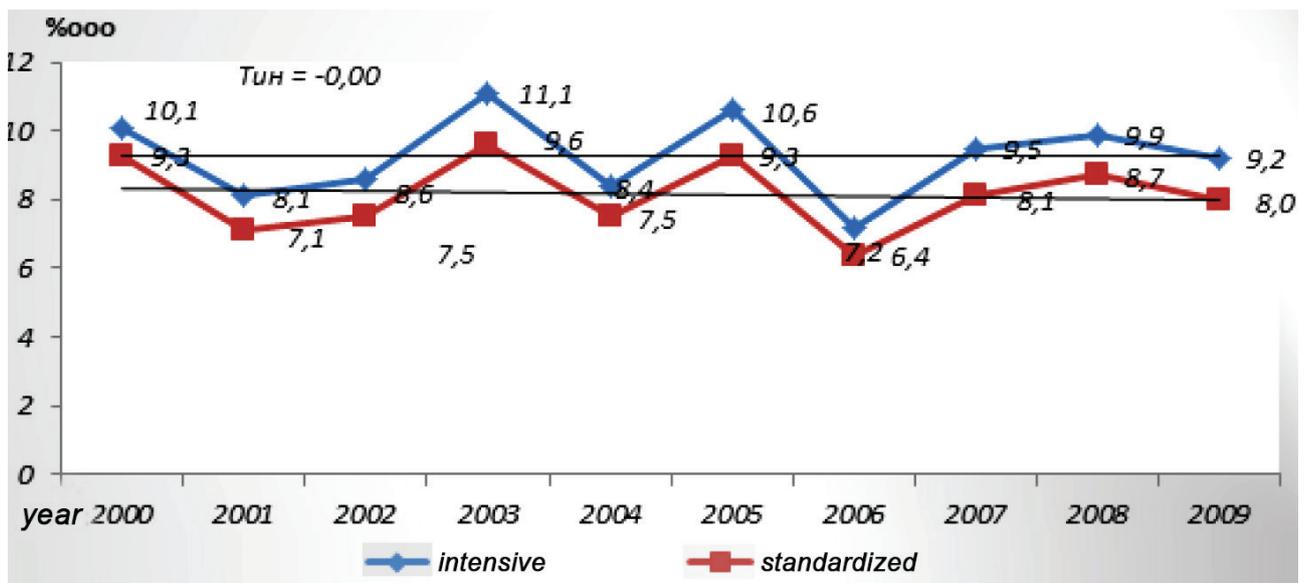


Figure 1 - Intensive and standardized indicators of RC incidence in Akmola region

RC epidemiology in Karaganda region.

In the mentioned period, 1201 cases of RC were registered in Karaganda region amounting to 3.7% of all malignant tumours. The incidence rates were growing with the age: from 0.2 at the age of 30 to 54.9 at the age of 70 and above (both sexes). The highest incidence was at the age of 70 and above (89.8 in men and 40.0 in women), and at the age of 60-69 (60.8 in men and 30.2 in women).

The dynamics of intensive indicators showed an increase from 8.7 to 11.2 by 2007, with a slight decrease to 9.2 by the end of the study. The standardized indicators for men changed from 11.7 to 12.7 and 9.6, respectively. The intensive incidence was $T_{in} = 0.2$, the standardized $T_{st} = 0.1$. The intensive and standardized indicators per 100,000 have increased during the period from 8.1 to 9.2.

The share of RC by age group was growing unimodally with the peak at the age of 60-69 (36.2%). The value for men was 38.4%, and for women – 34.0%. The total average annual intensive registered incidence of RC was 8.9 ± 0.5 , with the standardized value of 7.8 ± 0.5 per 100,000.

RC epidemiology in Qostanay region.

During the study period, 1112 cases of RC were registered in Qostanay region (5.0%). The incidence was growing by age. Before 50 years old, the incidence was low – below 20 per 100,000 for both sexes, with a noticeable increase in incidence at the age of 50-59 (24.2 in men, and 21.2 in women). The rates were high at the age of 60-69 and 70-79 years (59.0 and 69.0 for both sexes, respectively). Men aged 70-79 had the highest rate – 105.7 per 100,000 of the corresponding population.

In the dynamics, the incidence was fluctuating from 11.5 to 14.0 with a subsequent drop to 11.5, with 13.4, 15.8, and 11.0 in men. In women, the rate has slightly decreased from 13.3 to 12.0 per 100,000.

Thus, the specific share of RC was high in the age group of 60-69 years (35.3%) and was growing unimodally. The total annual average intensive incidence was 12.1 ± 0.4 , the standardized (world) incidence – 9.6 ± 0.4 .

RC epidemiology in North Kazakhstan region.

776 cases of RC were registered in North Kazakhstan amounting to 4.6% of all malignant tumours. In the age of group of 0-29, the incidence was 0.2 for both sexes, at the age of 30-39 – 1.3 to 3.1. At the age of 40-49, the incidence in men (7.4) was much higher than in women (5.1), with a significant growth at the age of 50-59 (20.5 in men, and 19.0 in women). At the age of 60-69 and 70 years old and above, the level was high in both sexes – 57.2 and 58.6, respectively. At that, the incidence in men was nearly twice higher than in women.

The intensive incidence has increased from 9.1 to 11.9, with a more growth in men. The standardized rates in men were also generally growing in dynamics. The highest peak of RC incidence was in 2006 (15.7). The standardized indicators have reached 16.1 that year; with a future decrease to 13.7 by the end of the study. The rates of the intensive and standardized indicators were similar. The age structure of men population in the region coincides with the world standard. The intensive and standardized indicators in female population of the region has grown in dynamics from 9.5 to 14.5 in 2005, and decreased to 10.1 by the end of the period. In general, the annual average intensive incidence was 11.6 ± 0.7 , the standardized (world) incidence – 9.3 ± 0.6 .

In dynamics, the intensive indicators for both sexes were decreasing up to 7.7 by the end of the study, with some growth in the beginning (9.3 to 9.8 in 2005). The rates of the intensive ($T_{in} = -0.1\%$) and standardized ($T_{st} = -0.1\%$) indicators were similar. The dependence of the indicators on sex was the same. In general, the annual average intensive incidence of RC was 7.5 ± 0.5 , the standardized (world) incidence – 8.8 ± 0.4 .

RC epidemiology in the city of Astana.

During 10 years, 395 cases of RC were registered in Astana amounting to 4.0% of all malignant tumours. The age-related indicators were growing from 0.2-

0.3 at the age of 0-29 to 0.9-1.1 at the age of 30-39. At the age of 40-49, the incidence was high among women (4.6) in comparison to men (1.2). Starting from the age of 50, the incidence in men was prevailing. The incidence was high at the age of 60-69: 65.5 in men vs. 38.4 in women, with the highest incidence at the age of 70+ for both sexes: 112.2 in men and 60.8 in women. Thus, the annual average intensive incidence of RC was 7.5 ± 0.4 , the standardized (world) incidence – 8.8 ± 0.4 .

Conclusion. Thus, 3185 cases of RC were registered in 10 years in the northern and central parts of Kazakhstan amounting to 4.3% of all malignant tumours. The annual average incidence in the region in total was 9.06, with the standardized rate of 8.62 per 100,000. There are certain sex- and age-related differences in prevalence and dynamics of intensive and standardized rates of RC. Age groups of 50-59, 60-69 and 70+ have quite high incidence rates. Geographical differences in the prevalence of RC are due to the age, ethnical structure and uneven impact of environmental factors, and require further epidemiological analytical studies.

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ESOPHAGEAL CANCER

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Epidemiology of esophageal cancer in the Republic of Kazakhstan in 2006-2015

Esophageal cancer ranks 10 among cancer pathologies. Kazakhstan has registered more than 1,300 cases of esophageal cancer each year and about 1,000 deaths from this type of cancer.

Purpose of the study: the incidence of esophageal cancer in the Republic of Kazakhstan in 2006-2015 for the purpose of target anti-cancer activities.

Materials and methods: The study included processing of data of all the patients with esophageal cancer registered in the Republic of Kazakhstan in 2006-2015. The dynamics of esophageal cancer incidence in men and women was studied in 10-years' time intervals and age intervals.

Basis for the study was the statistical data of the RK Agency on the number, sex-, age- and ethnic structure of population by the regions of the country. Standardization was done using direct method and world population.

Results and conclusions: During the studied period, the share of esophageal cancer among all the malignant tumours in the Republic of Kazakhstan amounted to 2.3%. The intensive incidence during 10 years were changing in dynamics from 9.3‰ in 2006 to 9.6‰ in 2007, with a decrease starting from 2007 to reach 7.7‰ by the end of the study.

The leading regions in esophageal cancer incidence were the Qyzylorda (17.2‰) and West Kazakhstan (17.1‰) regions. High incidences were also registered in Aktobe (13.1‰), Atyrau (12.2‰), and Mangistau (11.5‰) regions.

The lowest esophageal cancer incidences were registered in the cities of Almaty (4.4‰) and Astana

(4.9‰), the Almaty (5.8‰) and South Kazakhstan (6.8‰) regions and some northern areas of Kazakhstan.

Keywords: esophageal cancer, morbidity, mortality, intensive indicators.

In 2015, esophageal cancer ranked 10th in the structure of cancer pathologies. Esophageal cancer is one of the 5 main causes of death from cancer, and the main cause of death in 900,000 fatal cases [1, 2].

During the 10 years of study, 13354 cases of esophageal cancer were registered in Kazakhstan what amounts to 2.3% of all the malignant tumours [3, 4].

The analysis showed an upward trend of average annual intensive incidence rates of esophageal cancer in the RK in different age groups in dynamics in the studied period. No cases were registered at the age of 00-29 for both sexes. In the age group of 30-39, the incidence showed an average increase from 0.4‰ in 10 years. The incidence in the age group of 40-49 amounted to: 2.6‰ among women, 4.4‰ among men, and 3.5‰ for both sexes. In the age group of 50-59, the incidence of esophageal cancer has grown from 9.1‰ to 22.9‰. The growth of incidence of this cancer in the age group of 60-69 has been significant: 65.7‰ among men, and 32.4‰ among women per 100,000.

Age-related indicators of esophageal cancer incidence among male and female population of Kazakhstan have grown during the study period due to the population growth. The peak of incidence was in the age groups of 60-69 and 70+, with bimodal growth pattern (Fig. 1).

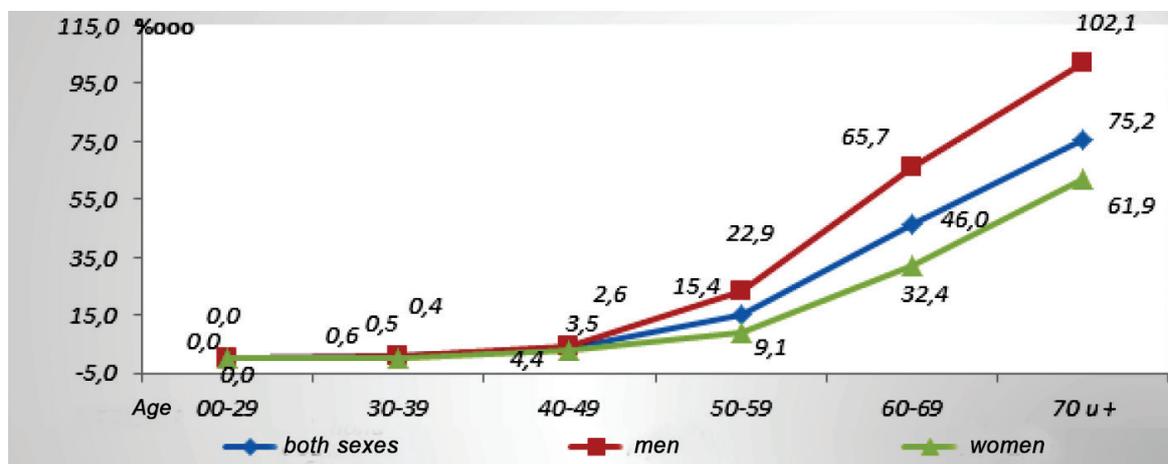


Figure 1 – Average annual sex- and age-related intensive incidence indicators of esophageal cancer in the RK, 2006-2015

The intensive incidence during 10 years were changing in dynamics from 9.3‰ in 2006 to 9.6‰ in 2007, with a decrease starting from 2007 to reach 7.7‰ by the end of the study (Fig. 2).

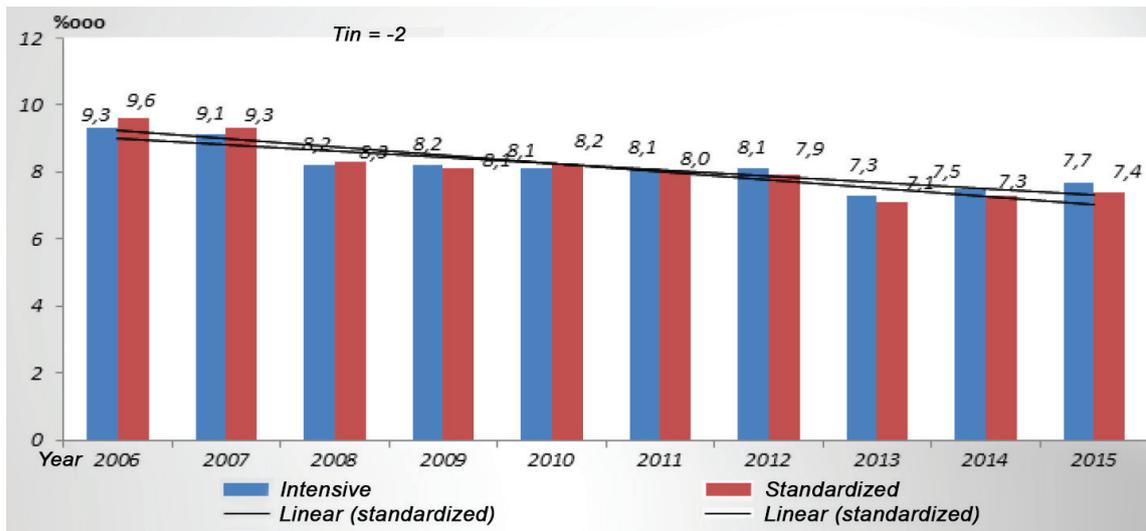


Figure 2 – Intensive and standardized incidence indicators of esophageal cancer in the RK, 2006-2015

Intensive and standardized indicators of incidence of esophageal cancer in the male population tended to decrease during the study period to reach 9.0‰ in 2015 vs. 10.3‰ in 2006, at the beginning of the study

(Fig. 3). The rates of intensive and standardized indicators of incidence did not coincide. The age structure of the national population did not coincide with the world standard.

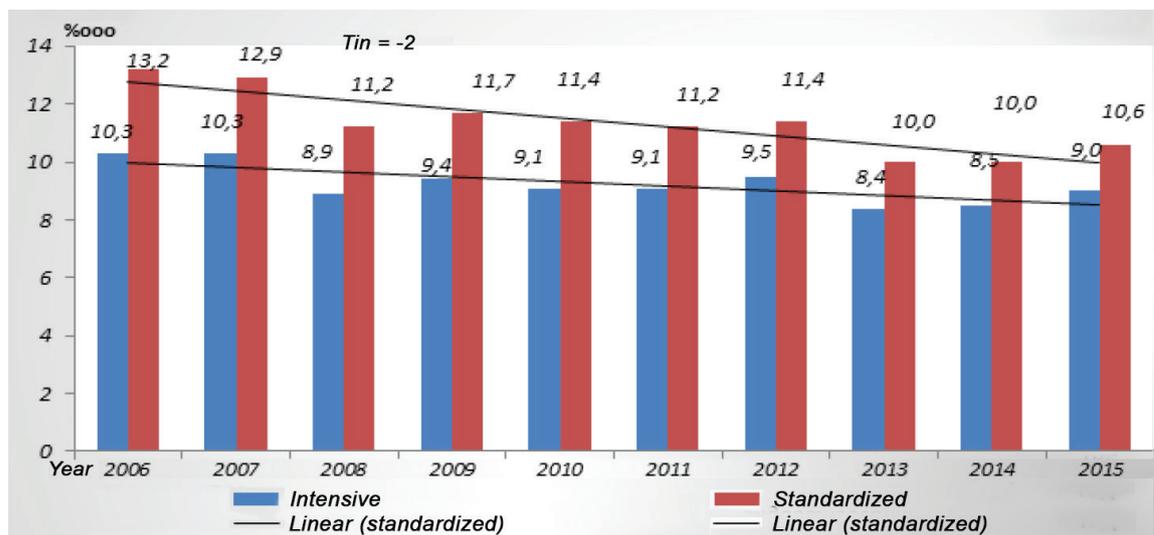


Figure 3 – Intensive and standardized incidence indicators of esophageal cancer among male population of the RK, 2006-2015

Among women, the indicators have decreased in 2006-2015 from 8.5‰ in the beginning of the period to 6.5‰

in the end of the study (Fig. 4). The rates of intensive and standardized indicators of incidence coincided.

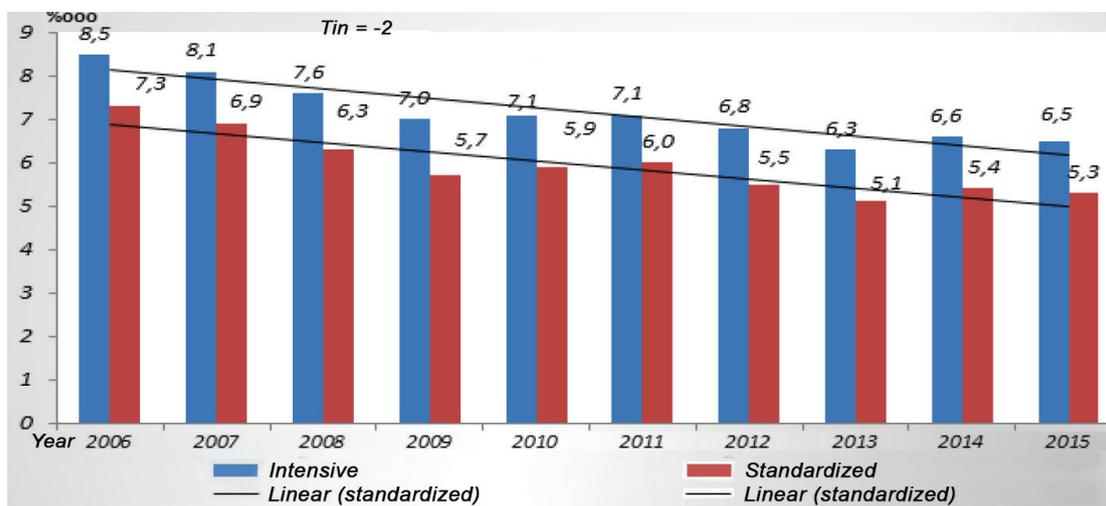


Figure 4 – Intensive and standardized incidence indicators of esophageal cancer among female population of the RK, 2006-2015

High share of esophageal cancer in all population of the RK (Fig. 5) was growing in all the age groups. In the age group of 60-69, the share among men (32.8%) was

higher than among women (28.1%). The peak was in the age group of 70+ among women (52.1%) while the share among men in that age group amounted to 35.5%.

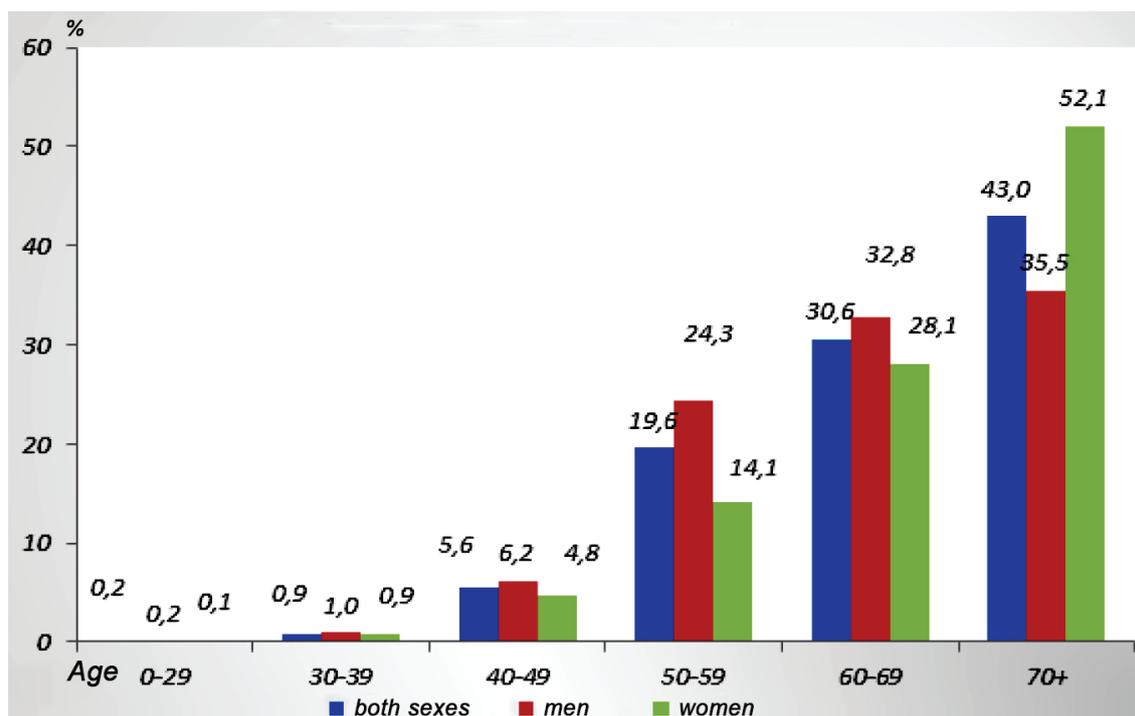


Figure 5 – The share of esophageal cancer by age groups in the RK, 2006-2015

The total annual average intensive incidence of esophageal cancer in Kazakhstan was equal to $8.2 \pm 0.2\text{‰}$, with the standardized (world) incidence of $8.1 \pm 0.3\text{‰}$.

Conclusions: Qyzylorda (17.2‰) and West Kazakhstan (17.1‰) regions were leading in esophageal cancer incidence. High incidences were also registered in Aktobe

(13.1‰), Atyrau (12.2‰), and Mangistau (11.5‰) regions.

The lowest esophageal cancer incidences were registered in the cities of Almaty (4.4‰) and Astana (4.9‰), the Almaty (5.8‰) and South Kazakhstan (6.8‰) regions and some northern areas of Kazakhstan (Fig. 6).

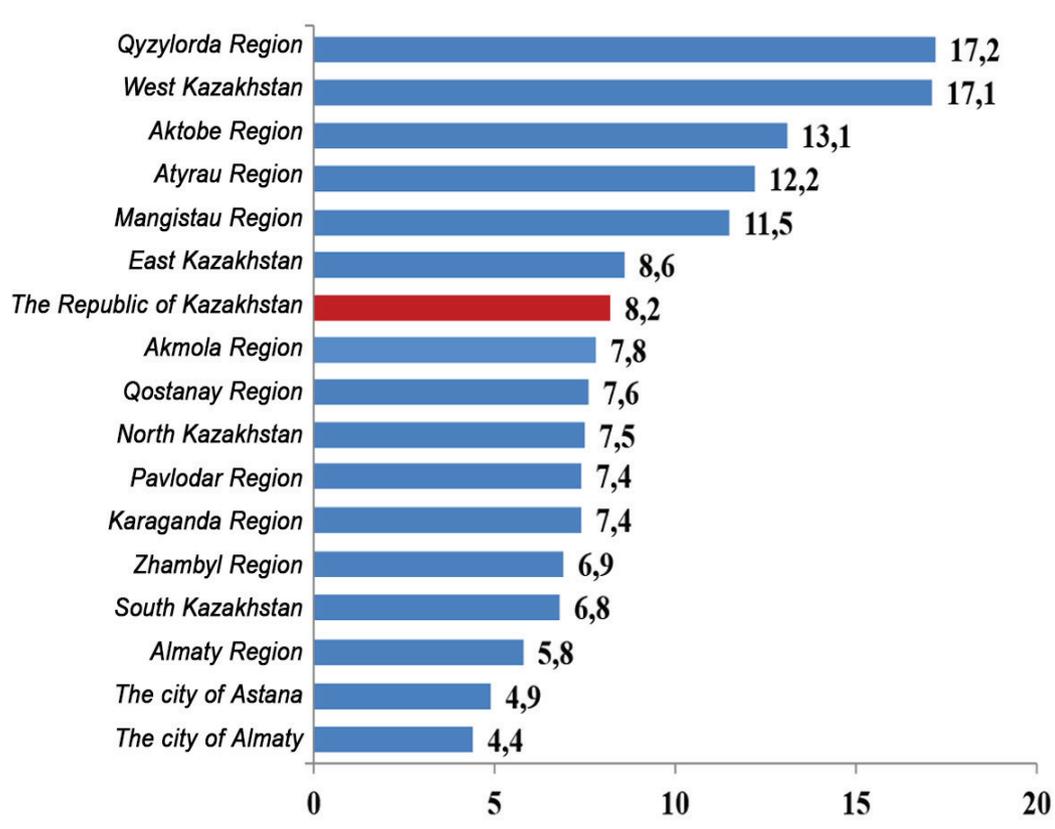


Рисунок 6 – Среднегодовые показатели заболеваемости раком пищевода по областям РК за 2006-2015 годы

Age-related specifics of prevalence of esophageal cancer in the RK in the studied period were characterized by the tendency towards an increase in the incidence rate in dynamics in the age groups of 60-69 and 70+ and a bimodal pattern of growth.

The analysis of age- and sex-related incidence in the RK during 10 years (2006-2015) showed an age-dependant incidence rate in dynamics, that is, the incidence of esophageal cancer was growing with the age.

In this paper, we were not considering the ethnical structure of the RK population though the ethnical factor had a certain influence on the incidence of some forms of cancer, especially, esophageal cancer, in Kazakhstan. Regional differences caused the peculiarities of the nature of nutrition due to differences in customs, habits of the peculiarities of the everyday life of the population living in certain regions of the Republic of Kazakhstan. Those differences have undoubtedly influenced the incidence of esophageal cancer. The incidence of esophageal cancer was higher in the regions where people mainly consumed

food rich in starch (bread, potato, ground corn products) and lacked animal protein, milk, fresh vegetables and fruits. Demographic changes in the population, its regional differences were the main factors affecting the incidence of malignant tumours in general, and of esophageal cancer in Kazakhstan in particular.

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«Это касается каждого на планете. Мы все хотели бы, чтобы наша жизнь и жизнь тех, кого мы любим, завершилась гармонично и спокойно.»

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КАЗАХСТАНСКАЯ АССОЦИАЦИЯ ПАЛЛИАТИВНОЙ ПОМОЩИ



Паллиативная помощь – активно развивающаяся во всем мире отрасль медицины, целью которой является улучшение качества жизни людей, находящихся в тяжелом состоянии вследствие серьезного заболевания. Эта цель достигается путем облегчения страданий пациента, благодаря правильной оценке и купированию боли и других тягостных физических симптомов, а также оказанию психологической, социально-юридической и духовной поддержки пациентов и их семей.

Миссия Ассоциации - это консолидация всех сил казахстанского общества с тем, чтобы каждый житель Казахстана, столкнувшийся с неизлечимым заболеванием, имел возможность реализовать свое право на достойную и максимально активную жизнь, без боли и страданий.

