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THE EFFECT OF THE EXTENT OF SURGERY AND LYMPH NODE DISSECTION ON THE DEVELOPMENT OF METACHRONOUS PERITONEAL DISSEMINATION IN GASTRIC CANCER

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ABSTRACT

Relevance: *Metachronous peritoneal dissemination (MPD) is among the top factors in the structure of gastric cancer (GC) progression, considerably worsening radical surgery outcomes. Since cancer cell dissemination in the peritoneal cavity is often triggered during surgery, assessing its role in MPD development is important.*

The study aimed to *assess the effect of the extent of radical surgery and lymph node dissection on the MPD development in radically operated gastric cancer patients.*

Methods: *The results of radical surgery performed on 1080 patients with gastric cancer (pT1-4N0-3M0) without spreading to the esophagus were assessed (647 males and 433 females) depending on the extent of surgical treatment (proximal/distal subtotal gastric resection (SGR), n=639/gastrectomy (GE), n=334; standard/combined surgery, n=973/107) and the extent of lymph node dissection (LD) – D1 (n=151) or D2 (n=929). Also assessed were survival rates (Kaplan-Meyer multiplier estimation method), cumulative incidence (CI) of competing events – MPD, metastases of other localizations, and mortality cases unrelated to gastric cancer (competing risks analysis).*

Results: *The analysis showed a statistically significant increase in the cumulative incidence (CI) of GC progression after combined operations (55.6±4.9%) as compared with the standard radical treatment (GE – 42.3±2.7%, SRG – 25.6±1.7%, respectively), including an increase in MPD CI in each of applied surgical procedures: after combined operations – 36.8±4.7%, after standard GE – 21.6±2.3% and after SRG – 11.1±1.2% (p_{Gray}<0.001). In the presence of lymphohematogenous metastases of other localizations, the relevant figures were 9.4±2.9% after combined operations, 9.3±1.6% after standard GE, and 5.0±0.9% after SRG (p_{Gray}=0.022). Lymph node metastases increased MPD CI after LD D1 from 8.3±2.8% (pN0) to 29.1±6.2% (pN1-3) (p_{Gray}<0.05), and after LD D2 – from 9.4±1.3% (pN0) to 27.3±2.1% (pN1-3) (p_{Gray}<0.05).*

Conclusions: *It is advisable to assess the extent of the planned surgical treatment and the condition of local lymph nodes when evaluating the probability of MPD development. The applied lymph dissection procedure did not affect the GC CI progression, including MPD development.*

Keywords: *gastric cancer, metachronous peritoneal dissemination (MPD), cumulative incidence (CI), surgical treatment.*

Introduction: According to A. Agnes et al., the combination of standard stages of rT (pT3-4) and pN (pN2-3) gastric cancer (GC) has a consequence of the risk of metachronous peritoneal dissemination (MPD) of the order of 30% [1]. In this case, exfoliation of tumor cells from the surface of the serous membrane and lymphogenic spread of tumor cells along the subperitoneal lymph plexus will be possible mechanisms [2, 3]. These factors contribute to the dissemination of tumor cells in the peritoneal cavity before the start of surgical treatment. Unfortunately, they are not limited to the list of all possible mechanisms of MPD, which has a high proportion in the structure of GC progression [1, 2, 4]. In particular, assessing the probability of progression of GC ignores the possibility of dissemination of tumor cells during the mobilization of the stomach and lymph dissection (LD) [1, 5]. This research is devoted to assessing the impact of the extent of surgery on its long-term results in the context of the possibility of further progression.

The study aimed to evaluate the effect of the extent of radical surgery and lymph dissection on MPD development in radically operated gastric cancer patients.

Materials and Methods: The material for the research was the data of 1080 patients who have undergone radical surgery for GC (rT1-4N0-3M0) without spreading to the esophagus (647 men and 433 women). In these patients, neoadjuvant and adjuvant treatment was not carried out according to the standards in force in the Republic of Belarus in 2012-2018 [6]. The choice of this cohort was due to the need to determine the features of the structure of GC progression in patients who have undergone radical surgery under the condition of different extent of surgeries and LD but in the absence

of the influence of antitumor drug treatment aimed at preventing the development of various variants of GC progression.

The research assessed the effect on the development of MPD of the extent of radical surgery (proximal/distal subtotal gastric resection (SGR), n=639/gastrectomy (GE), n=334; standard/combined surgery, n=973/107) and the extent of LD – D1 or D2. LD in D2 was performed in 929 patients and included monoblock removal of fiber together with lymph nodes of stages I-II of metastasis according to the recommendations of the Japanese Association for the Study of GC [7]: Stage I (N1) – perigastric lymph collectors (No. 1-6); Stage II (N2) – lymph nodes located along the branches of the celiac axis (left gastric (No. 7), common hepatic (No. 8) and splenic (No. 11) arteries), the celiac axis (No. 9), in the splenic hilum (No. 10), as well as lymph nodes of the hepatoduodenal ligament (No. 12). LD in D1 was performed in 151 patients and included removal of lymph nodes of the first stage of metastasis, as well as lymph nodes of the left gastric artery (No. 7).

The assessment of long-term treatment outcomes included the calculation of the following survival rates:

Overall survival (OS) – the events included deaths from cancer-related causes, antitumor treatment, or a concomitant pathology.

Adjusted survival rate (AS) – the events included deaths caused by underlying diseases.

Progression-free survival (PFS) – the events included GC progression and deaths from GC-associated causes.

Dissemination-free survival (DFS) – the events included tumor dissemination along the peritoneum and deaths from GC-associated causes.

Survival was assessed with a standard error (SE) using the Kaplan-Meyer multiplier method (comparative survival analysis by log-rank test). SE was calculated using the Greenwood formula. The monitoring was considered complete when a relevant event was reported; in other cases, the monitoring was «censored.»

The study assessed the cumulative incidence (CI) of competing events: CI of MPD and CI of distant lymphohematogenous metastases (DLHM) (in cases when MPD and DLHM were the only variants of distant metastases at the time of confirmation of GC progression); CI of a combination of MPD and DLHM; CI of deaths from causes not related to GC progression; CI of deaths from complications of treatment. The competing nature of the above events suggests the inevitability of the occurrence of one of them as the first during the period after the completion of radical treatment.

The assessment of CI of various events mentioned above used the analysis of competing risks [8]. The incidence for different groups was compared using the Gray test (p_{Gray}) [9]. When identifying the general heterogeneity by the log-rank test, posterior (post-hoc) pairwise analysis of groups with Holm's correction for multiple comparisons was carried out.

Statistical data analysis was performed using the GC statistical package. 3.1.1 (GPL license) using *survival* [10] and *cmprsk* [11] packages.

Results: The median follow-up in the sample under consideration was 97 months.

An increase in the extent of surgery from standard radical GRF to standard radical GE and, for a more common tumor process, to combined operations was accompanied by decreased survival rates (Table 1).

Table 1 – Five-year survival in groups with different types of surgery

Test criterion	Survival rates			
	OS (%±SE)	AS (%±SE)	PFS (%±SE)	DFS (%±SE)
Type of surgery				
Gastrectomy, n=334	47.4±2.7#	58,5±2.9#	53.9±2.9#	55.8±2.9#
Combined operations*, n=107	31.3±4.5†	40.0±5.2†	36.9±5.1†	39.5±5.2†
Subtotal gastric resection**, n=639	64.5±1.9	76.2±1.8	72.5±1.8	74.3±1.8
$p_{log\text{-}rank}$	<0.001	<0.001	<0.001	<0.001
Extent of lymph dissection				
D1, n=151	51.0±4.1	68.9±4.1	65.7±4,2	67.5±4.2
D2, n=929	56.8±1.6	67.2±1.6	63.2±1,7	65.0±1.6
$p_{log\text{-}rank}$	0.04	0.826	0.551	0.519

Notes:
When the DFS indicators are calculated, the development of MPD, both isolated and in combination with DLHM, was taken into account as an event;
* – combined gastrectomy/subtotal gastric resection;
** – proximal/distal subtotal gastric resection;
# – statistically significant differences in post-hoc pair-wise comparisons between the group of patients who have undergone gastrectomy and the rest with Holm's correction;
† – statistically significant differences in post-hoc pair-wise comparisons between the group of patients who have undergone combined operations and the rest with Holm's correction

The expected worse treatment results with low survival rates and high CI of GC progression were reported in the group of patients who have undergone combined operations and were due to both a more common pT4b tumor process and a higher CI of treatment complications in these patients compared to the

cohort in which standard operations have been performed (Table 1, 2):

1) a more common tumor process that usually requires GE (in comparison with SGR), as well as combined operations, which resulted in a more frequent progression of the tumor process, where CI was 42.3±2.7% and 55.6±4.9%, respectively, exceeding that for SGR (25.6±1.7 (p_{Gray}<0.001);

2) a higher incidence of complications and the associated CI of deaths from complications of treatment after performing GE and combined surgery, i.e., 3.6±1.0% and 4.7±2.1%, respectively, compared to GRF 11.0±1.2% (p_{Gray}=0.006).

Previously, a similar dependence of survival on the extent of surgery performed was described by J. Deng et al. (2015) [12] and FF. Chen et al. (2016) [13].

A detailed analysis of the progression structure established that an increase in MPD CI was the main reason that harmed the long-term results of treatment after performing combined operations (Table 2).

Table 2 – Five-year cumulative incidence of variants of gastric cancer progression and cases of mortality not related to the progression of the tumor process in groups with different types of surgery

Type of surgery	Five-year cumulative incidence (%±SE)			
	MPD	DLHM	MPD +DLHM	Deaths from non-oncological pathologies and treatment complications
Gastrectomy, n=334	21.6±2.3#	11.4±1.7	9.3±1.6#,‡	13.5±1.9
Combined operations*, n=107	36.8±4.7†	9.4±2.8	9.4±2.9	15.0±3.5
Subtotal gastric resection**, n=639	11.1±1.2	9.1±1.1	5.0±0.9	12.4±1.3
p_{Gray}	<0.001	0.657	0.022	0.757

Notes:
* – combined gastrectomy/subtotal gastric resection;
** – proximal/distal subtotal gastric resection;
# – statistically significant differences in post-hoc pair-wise comparisons between the group of patients who have undergone gastrectomy and the rest;
† – statistically significant differences in post-hoc pair-wise comparisons between the group of patients who have undergone combined operations and the rest of the groups:
‡ – statistically significant differences in post-hoc pair-wise comparisons between the patients who have undergone gastrectomy and those who have undergone subtotal gastric resection.

The latter can be explained by the more intensive dissemination of tumor cells in the peritoneal cavity in the case of combined operations compared to standard ones, which is due not only to the more intensive dissemination of cells from the tumor surface but also to the dissemination of cells from metastatically altered regional lymph nodes. Thus, the extent of surgery performed allows us to consider a possible variant of GC progression, particularly MPD, and can be used to assess the likelihood of progression.

Comparison of groups with different LD extent did not reveal statistically significant differences in survival functions and progression CI (Table 1, 3), which corresponds to the literature data stating that there is no clear relationship between the increase in LD extent and the frequency of GC progression, in particular, MPD [14].

Table 3 – Five-year cumulative incidence of adverse events in groups with different extent of lymph dissection

Extent of lymph dissection	Five-year cumulative incidence (%±SE)		
	gastric cancer progression	deaths from treatment complications	deaths from non-oncological pathologies
D1, n=151	29.8±3.7	4.6±1.7	16.6±3.0
D2, n=929	34.3±1.6	1.9±0.5	9.6±1.0
Gray test	0.229	0.331	0.002

Attention is drawn to the statistically significant increase in CI of deaths from non-oncological pathology in the group of patients with D1 LD, which is explained by the implementation of this reduced extent of LD in patients with concomitant pathology, which is often competitive in comparison with the underlying disease.

However, the assessment of CI of the considered variants of progression in the pN+ and pN0 groups revealed an increase in CI of MPD in patients with lesions of regional lymph collectors, regardless of the variant of MPD (Table 4), which confirms the results of several studies demonstrating the possibility of increasing the frequency of MPD if LD is performed in patients with pN+ and the absence of adjuvant intraperitoneal chemotherapy [4, 15].

Thus, the development of MPD does not depend on the variant of LD (D1 or D2) but on the presence of a metastatic lesion of regional lymph collectors when LD (as a mandatory component of radical treatment) causes intraoperative dissemination of tumor cells.

Table 4 – Five-year cumulative incidence of variants of gastric cancer progression and cases of mortality not related to gastric cancer in groups with different extent of lymph dissection

Extent of lymph dissection; state of regional lymph nodes pN	Five-year cumulative incidence (%±SE)			
	MPD	DLHM	MPD+DLHM	deaths from non-oncological pathology and treatment complications
D1–pN0, n=96	8.3±2.8*†	8.3±2.8	0	19.8±4.1***
D2–pN0, n=488	9.4±1.3‡	3.9±0.9‡	3.1±0.8‡	11.7±1.5
D1–pN1-3, n=55	29.1±6.2**	20.0±5.5	1.8±1.8	23.6±5.8§
D2–pN1-3, n=441	27.3±2.1	15.5±1.7	11.1±1.5	11.6±1.5
p_{Gray}	<0.001	<0.001	<0.001	0.002

Notes:
* – for pairwise comparisons, groups D1– pN0 and D2–pN0 do not differ;
** – for pairwise comparisons, groups D1–pN1-3 and D2–pN1-3 do not differ;
† – Statistically significant differences in post-hoc pair-wise comparisons between group D1–pN0 and groups D1–pN1-3, D2–rN1-3;
‡ – Statistically significant differences in post-hoc pair-wise comparisons between group D2–pN0 and groups D1–pN1-3, D2–rN1-3;
*** – statistically significant differences in post-hoc pair-wise comparisons between group D1–N0 and group D2–rN1-3;
§ – statistically significant differences in post-hoc pair-wise comparisons between group D1–pN1-3 and group D2–N1-3.

In connection with the above, assessing the probability of MPD should consider both the extent of surgery and the presence of metastatic lesions of regional lymph nodes (pN+). The latter may be associated with such characteristics of the tumor process as an infiltrative form of primary tumor growth, a non-adhesive variant of adenocarcinoma, subtotal gastric lesion, etc. In other words, developing prognostic models requires comprehensive consideration of several potential predictors of poor prognosis.

Discussion: The analysis of survival rates, which is traditional for oncological studies, indicates that it needs to be more informative to clarify the influence of certain factors, particularly the extent of surgery and LD, on the structure of GC progression, including its variants. It is due to the lack of the possibility of distinguishing cases of mortality unrelated to the underlying disease (in this case, to GC), e.g., when calculating the indicators of OS. The second reason for the lack of information content is the need for more possibility of distinguishing specific progression variants, which implies taking into account the occurrence of various localizations of metachronous distant metastases, particularly MPD.

The analysis of competing risks carried out in this study made it possible to determine the CI of various GC progression variants for a more accurate picture of the factors (in this case, the extent of surgery and LD) responsible for the development of a particular variant of progression, and separating them from lethality not related to GC progression. It has been established that the development of MPD, where CI prevails in the progression structure, is the main variant of progression that determines the poor prognosis after performing radical surgeries, both in the standard and combined variants. According to the literature, the assessment of the effect of the extent of surgery on the frequency of MPD after treatment of GC needs to be clarified. In particular, according to Kang L.-Y. et al. (2013) [16], there were no differences in the number of disseminated peritoneal lesions in the long term after standard radical and combined surgeries. On the contrary, the results of our research demonstrated a high frequency of MPD, which occupies a leading position in the structure of cases of GC progression after combined operations. It was also reported that the number of MPD cases in the follow-up dynamics is determined not by the LD variant but by the presence of a metastatic lesion of regional lymph collectors. The latter requires adjuvant intraperitoneal chemotherapy to eliminate tumor cells disseminated in the peritoneal cavity.

Thus, the analysis of CI of GC progression variants shows a relative radicality of surgical treatment when the tumor process extends beyond the stomach. This is due to a high probability of metachronous distant metastases, MPD being their most common variant. All of the above justifies the need to develop and administer adjuvant treatment (e.g., intraperitoneal chemotherapy) to prevent carcinomatosis long after radical surgery. At the same time, it is more rational to supplement the standard extent of therapeutic measures with intraperitoneal chemotherapy under an individual approach with an assessment of the likelihood of MPD development based on the predictors of possible GC progression, which may include both the extent of surgery and clinical and morphological features of the tumor process (pN+ and associated morphological characteristics of the primary tumor).

Conclusions:

1. The conventional approach with the assessment of survival rates does not allow for determining the impact of the extent of surgery on the nature of the progression of the tumor process, which determines the feasibility of using the approach based on the assessment of the cumulative incidence of competing events which, for locally advanced GC, maybe metachronous peritoneal dissemination and its combination with distant lymphohematogenous metastases, deaths from complications of treatment and deaths from concomitant pathology.

2. An advanced tumor process requiring combined operations causes a statistically significant increase in the 5-year cumulative incidence of progression (55.6±4.9%) as compared with standard radical treatment (42.3±2.7% after GE, 25.6±1.7% after GRP), including an increase in 5-year CI of metachronous peritoneal dissemination in an isolated variant (36.8±4.7% after combined operations and 21.6±2.3% and 11.1±1.2% after standard GE and GRF, respectively (p_{Gray}<0.001) and combination with distant lymphohematogenous metastases of other localization (9.4±2.9% after combined operations or 9,3±1,6% and 5,0±0,9% after standard GE and SGR, respectively (p_{Gray}=0.022).

3. The variant of the performed lymph dissection does not affect the cumulative incidence of gastric cancer progression, which is 29.8±3.7% after D1 LD, 34.3±1.6% after D2 LD (p=0.229), including the cumulative incidence of metachronous peritoneal dissemination, which is 15.9±3.0% and 17.0±1.2% after D1 and D2 dissections, respectively (p=0.530).

4. Metastatic lesion of regional lymph collectors caused more frequent tumor progression during D1 and D2 dissection. In contrast, the 5-year CI of progression for D1 and D2 LD was 52.7±6.9% and 53.9±2.4%, respectively, for patients with rN1-3, exceeding similar indicators for patients with pN0 – 16.7±3.8% and 16.6±1.7% (pGray<0.001), including MPD CI after D1 LD – 8.3±2.8% at pN0 to 29.1±6.2% at rN1-3 (pGray<0.05); after D2 LD 9.4±1.3% at pN0 to 27.3±2.1% at pH1-3 (pGray<0.05).

5. It seems relevant to develop risk assessment models for an individual approach to the scope of antitumor treatment to prevent MPD. Considering the extent of surgery and the condition of regional lymph collectors is reasonable when assessing the MPD probability.

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АҢДАТПА

ОПЕРАЦИЯ МЕН ЛИМФОДИССЕКЦИЯ КӨЛЕМІНІҢ АСҚАЗАН ҚАТЕРЛІ ІСІГІНДЕГІ МЕТАХРОНДЫ ПЕРИТОНЕАЛЬДІ ДИССЕМИНАЦИЯНЫҢ ДАМУЫНА ӘСЕРІ

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Өзектілігі: *Метахронды перитонеальді диссеминация асқазан қатерлі ісігінің прогрессиясының құрылымындағы жетекші факторлардың бірі, бұл оны түбегейлі емдеу нәтижелерін айтарлықтай нашарлатады. Перитонеум қуысындағы ісік жасушаларының таралу процестері көбінесе хирургиялық емдеу процесінде басталады, олардың метахронды перитонеальді диссеминация дамуына әсерін бағалау маңызды.*

Зерттеудің мақсаты *– түбегейлі операция мен лимфодиссекция көлемінің асқазан қатерлі ісігімен ауыратын науқастарда метахронды перитонеальді диссеминацияның дамуына әсерін бағалау.*

Әдістері: *Орындалған операция көлеміне байланысты өңешке ауыспай (ерлер 647, әйелдер 433) асқазан обырына (pT1-4N0-3M0) түбегейлі операция жасалған 1080 пациенттің (асқазанның проксимальды/дистальды субтотальды резекциясы, n=639 / гастрэктомия, n=334) түбегейлі хирургиялық емдеу нәтижелеріне талдау жүргізілді; стандартты/аралас операция, n=973/107) және орындалатын лимфодиссекция көлемі – D1 (n=151) немесе D2 (n=929). Сондай-ақ, өмір сүру деңгейі (Каплан-Мейердің көбейту әдісі), шоғырланымдық инциденттінің – метахронды перитонеальді диссеминация, басқа локализацияның метастаздары, асқазан қатерлі ісігімен байланысты емес өлім жағдайлары (бәсекелес тәуекелдерді талдау) бағаланды.*

Нәтижелері: *Стандартты түбегейлі емдеумен салыстырғанда (гастрэктомиядан кейін 42,3±2,7%, асқазанның субтотальды резекциясынан кейін 25,6±1,7%) шоғырланымдық прогрессия инцидентінің статистикалық маңызды өсуі (55,6±4,9%) анықталды, оның ішінде оқшауланған нұсқадағы метахронды перитонеальді диссеминацияның шоғырланымдық инцидентінің жоғарылауы (аралас операциялардан кейін 36,8ұ4,7%, стандартты гастрэктомиядан және асқазанның субтотальды резекциясынан кейін сәйкесінше 21,6±2,3% және 11,1±1,2% (pGray<0,001)) және біріктірілген кезде метахронды перитонеальді диссеминация, басқа локализацияның алыс лимфогематогендік метастаздарымен (аралас операциялардан кейін 9,4±2,9%, стандарты гастрэктомия және асқазанның субтотальды резекциясы кейін сәйкесінше 9,3±1,6% және 5,0±0,9%, (pGray=0,022)) құрайды. Лимфа түйіндерінде метастатикалық зақымдануының болуы D1 лимфодиссекциясынан кейінгі метахронды перитонеальді диссеминацияның шоғырланымдық инцидентінің 8,3±2,8%-нен (pN0) 29,1±6,2%-ге дейін (pN1-3) (pGray<0.05) және D2 лимфодиссекциясынан кейін 9,4±1,3%-дан (pN0) жоғарылауына әкелді. 27,3±2,1%-ге дейін (pN1-3) (pGray<0.05).*

Қорытынды: *Даму ықтималдығын бағалау кезінде метахронды перитонеальді диссеминация операция көлемін және аймақтық лимфа түйіндерінің жағдайын бағалау ұсынылады. Қолданылған лимфодиссекция процедурасы метахронды перитонеальді диссеминацияның дамуын қоса алғанда, асқазан қатерлі ісігінің дамуының жиынтық жиілігіне әсер етпеді.*

Түйінді сөздер: *асқазан қатерлі ісігі, метахронды перитонеальді диссеминация, шоғырланымдық инцидент, хирургиялық емдеу.*

АННОТАЦИЯ

ВЛИЯНИЕ ОБЪЕМА ОПЕРАЦИИ И ЛИМФОДИССЕКЦИИ НА РАЗВИТИЕ МЕТАХРОННОЙ ПЕРИТОНЕАЛЬНОЙ ДИССЕМИНАЦИИ ПРИ РАКЕ ЖЕЛУДКА

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Актуальность: *Метахронная перитонеальная диссеминация (МПД) составляет высокий удельный вес в структуре прогрессирования рака желудка (РЖ), существенно ухудшая результаты его радикального лечения. Процессы диссеминации опухолевых клеток в полости брюшины зачастую запускаются в процессе выполнения хирургического лечения, что определяет целесообразность оценки их влияния на развитие МПД.*

Цель исследования *– оценить влияние объема радикальной операции и лимфодиссекции на развитие МПД у пациентов, радикально оперированных по поводу РЖ.*

Методы: *Проведен анализ результатов радикального хирургического лечения 1080 пациентов, радикально оперированных по поводу РЖ (pT1-4N0-3M0) без перехода на пищевод (мужчин 647, женщин 433) в зависимости от объема выполненной операции (проксимальная/дистальная субтотальная резекция желудка (СРЖ), n=639/гастрэктомия (ГЭ), n=334; стандартная/комбинированная операция, n=973/107) и объема выполняемой лимфодиссекции (ЛД) – D1 (n=151) или D2 (n=929). Оценены показатели выживаемости (метод множительных оценок Каплана-Мейера), кумулятивной инцидентности конкурирующих событий – МПД, метастазов другой локализации, случаев летальности, не связанной с РЖ (анализ конкурирующих рисков).*

Результаты: *Установлено статистически значимое увеличение кумулятивной инцидентности прогрессирования (55,6±4,9%) в сравнении со стандартным радикальным лечением (после гастрэктомий 42,3±2,7%, после СРЖ 25,6±1,7%), в том числе увеличение КИ МПД в изолированном варианте после комбинированных операций – 36,8±4,7% и после стандартных ГЭ и СРЖ – 21,6±2,3% и 11,1±1,2%, соответственно; p_{Gray}<0,001) и при сочетании МПД с отдаленными лимфогематогенными метастазами другой локализации (после комбинированных операций – 9,4±2,9% и после стандартных ГЭ и СРЖ – 9,3±1,6% и 5,0±0,9%, соответственно; p_{Gray}=0,022). Наличие метастатического поражения регионарных лимфоколлекторов обусловливает увеличение КИ МПД после ЛД D1 – с 8,3±2,8% (pN0) до 29,1±6,2% (pN1-3) (p_{Gray}<0,05); после ЛД D2 – с 9,4±1,3% (pN0) до 27,3±2,1% (pN1-3) (p_{Gray}<0,05).*

Заключение: *При оценке вероятности развития МПД целесообразной представляется оценка объема операции и состояния регионарных лимфоколлекторов. Вариант выполненной ЛД не влияет на кумулятивную инцидентность прогрессирования РЖ, включая развитие МПД.*

Ключевые слова: *рак желудка, метахронная перитонеальная диссеминация, кумулятивная инцидентность, хирургическое лечение.*

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