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Prognosis of distal diffuse gastric cancer depending on the extent of surgical procedure

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Abstract

Aim – to study the clinical and morphological characteristics and conduct a comparative assessment of the survival of patients with locally advanced distal diffuse gastric cancer depending on the type of the surgical procedure.

Material and methods. We performed a retrospective review of the impact of the extent of surgery in the prognosis of 125 patients with diffuse gastric cancer of distal localization, who underwent total gastrectomy or distal subtotal gastrectomy at the N.N. Blokhin National Medical Research Center of Oncology in the period from 2005 to 2022.

Results. The depth of tumor invasion (T4), the lymph node status, and the tumor stage had a significant negative prognostic value in the univariate analysis. Resection margin (R1) tended to significantly affect the overall survival ($p=0.082$). The extent of the surgical procedure did not affect overall survival in the univariate analysis ($p=0.75$). The multivariate analysis revealed that only the tumor stage had a relative effect on the overall survival. In the distal gastrectomy group, the median overall survival and the 5-year OS rates were 85.0 months, 58.8% (95% CI: 0.487-0.711). In the total gastrectomy group, the median overall survival, 5-year OS rates were 89.0 months,

60.3% (95% CI: 0.460-0.791). However, the differences were statistically insignificant ($p=0.75$). In patients in the distal subtotal gastrectomy group, the recurrence was detected in 12.7% of all cases of recurrence (8/63): 6 of them with intramural recurrence and 2 of them with intramural and distant recurrence of the disease. In patients in the total gastrectomy group, intramural recurrence was found only in one patient (4.8%) in the esophago-enteroanastomosis.

Conclusions. Overall survival and relapse-free survival rates in patients with diffuse cancer of distal localization after total and distal subtotal gastrectomy do not have significant differences. However, distal subtotal gastrectomy in this category of patients is associated with a higher risk of local recurrence (12.7%) and can not be recommended as an alternative to total gastrectomy in patients with satisfactory functional status.

Keywords: diffuse gastric cancer, distal subtotal gastrectomy, gastrectomy, prognosis.

Conflict of Interest: nothing to disclose.

Citation

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Прогноз при диффузном раке желудка дистальной локализации в зависимости от объема хирургического вмешательства

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Аннотация

Цель – изучить клинико-морфологические характеристики, провести сравнительную оценку выживаемости и частоты интрамурального рецидива опухоли у больных диффузным раком желудка дистальной локализации в зависимости от объема хирургического вмешательства.

Материал и методы. Проведен анализ влияния объема хирургического вмешательства на прогноз у 125 больных диффузным раком желудка дистальной локализации, которым в НМИЦ онкологии имени Н.Н. Блохина в период 2005-2022 гг. выполнена радикальная гастрэктомия (ГЭ) или дистальная субтотальная резекция желудка (ДСРЖ).

Результаты. При однофакторном анализе достоверное влияние на выживаемость имели глубина опухолевой инвазии (T4), статус пораженных лимфатических узлов, стадия опухолевого процесса. Тенденцию к статистически значимому влиянию на общую выживаемость имел край резекции ($p=0,082$). Объем выполненного хирургического вмешательства на общую выживаемость при однофакторном анализе влияния не оказывал ($p=0,753$). При многофакторном анализе было выявлено, что статистически значимое влияние на общую выживаемость имела только стадия опухолевого процесса. Медиана общей выживаемости, 5-летняя выживаемость в группе ДСРЖ составили 85,0 месяца, 58,8% (95% ДИ:

0,487-0,711). Медиана общей выживаемости, 5-летняя выживаемость в группе ГЭ составили 89,0 месяца, 60,3% (95% ДИ: 0,460-0,791). Различия в общей выживаемости статистически недостоверны ($p=0,75$). У пациентов в группе ДСРЖ интрамуральный рецидив выявлен в 12,7% случаев всех рецидивов (8/63): у 6 пациентов выявлен только интрамуральный рецидив в зоне гастрозентероанастомоза, а у двоих пациентов – интрамуральный рецидив и отдаленные метастазы. В группе пациентов, которым провели ГЭ, выявлен лишь 1 случай (4,8%) интрамурального рецидива заболевания в эзофагоэнтероанастомозе.

Заключение. Показатели общей выживаемости и безрецидивной выживаемости у больных диффузным раком дистальной локализации после ГЭ и ДСРЖ достоверных различий не имеют. Однако выполнение ДСРЖ у данной категории пациентов сопряжено с более высоким риском интрамурального рецидива опухоли (12,7%) и не может быть рекомендовано в качестве альтернативы ГЭ у больных с удовлетворительным функциональным статусом.

Ключевые слова: диффузный рак желудка, дистальная субтотальная резекция желудка, гастрэктомия, прогноз.

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РЖ – рак желудка; ПКР – перстневидноклеточный рак; ДСРЖ – дистальная субтотальная резекция желудка; ГЭ – гастрэктомия; БРВ – безрецидивная выживаемость; ОБ – общая выживаемость; ОР – отношение рисков; ДИ – доверительный интервал.

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INTRODUCTION

Morphologically diffuse gastric cancer (GC) is characterized with disorders in the intercellular adhesion without formation of glandular tissue, diffused spreading of the tumor cells in the walls of the stomach, more aggressive course of the neoplastic process and adverse survival outcomes as compared to the intestinal subtype of cancer. In the group of diffuse gastric cancer, the predominant histologic form is the signet ring cell carcinoma (SRCC) represented by isolated cells with a characteristic signet cell morphology and diffused growth pattern, which allows its reference to the diffuse GC (P. Lauren) [1-6]. According to the SEER register, in the period from 1975 to 2016 proportion of patients with SRCC is 16.8%. The diffuse subtype is more incident in women and young people, it is characterized with a more frequent dissemination in the

peritoneum, resistance to chemotherapy, and locally advanced tumor course by the moment of disease diagnosis [5, 7-9].

In the Japanese classification of gastric carcinoma, it is customary to refer to three sections of the stomach approximately similar in size: the upper third (proximal section), the middle third (corpus) and the lower part [10]. This conventional division of the stomach into three parts in surgical practice is only used to describe the tumor localization. It is to be emphasized that the sections of the stomach in the surgical classifications do not match those in the anatomical classifications. In Russia, distal GC is identified as a tumor involving only the antrum or the pylorus, in which, according to the clinical recommendations of the Russian Oncology Association, distal subtotal gastrectomy (DSG) is indicated. It is interesting to note that the involvement of the lower third

of the corpus in distal cancer may necessitate an extensive instead of a preserving surgery [11].

In Russia, in the cases of antrum diffuse GC, gastrectomy with D2 lymph node dissection is preferred as a standard surgical procedure, especially in young patients, since in this category of patients the possibility of recurrent cancer in the remaining part of the stomach remains high [8, 9, 12], and the lymph node dissection is less extensive in the preserving surgery as compared to the conventional gastrectomy. According to the data from 62 hospitals of Europe, in the cases of antrum diffuse GC, 44% of surgeons prefer the gastrectomy [12].

Lesser surgical trauma and more favorable outcomes of the restoration of nutritive status of patients after DSG raise no doubts and are used actively in the cases of intestinal adenocarcinoma of distal localization [13, 14].

According to the ESMO clinical recommendations, the major condition of the radically performed DSG is the absence of cancer cells along all margins of resection (R0). The margin for the proximal edge of resection in the diffuse GC is to be at least 5 cm, for the diffuse cancer is characterized with submucosal growth, which might be a technical difficulty to achieve 'clear' margins of resection. Thus, performance of DSG in the cases of distal GC may only be justified if the radical principles are met and there are no cancer cells along the resection margin [15].

As of today, there is no definitive consensus as to the extent of surgical intervention in cases of distal gastric cancer. The extent of surgery in distal gastric cancers is usually determined by the surgeon's preference and personal experience, as well as the patient's total physical condition [11, 12]. Thus, the effect of the extent of surgery on the prognosis of patients with diffuse distal gastric cancer remains a disputable and understudied problem.

MATERIAL AND METHODS

The study included 125 patients with diffuse gastric cancer of distal localization who had undergone radical or palliative total gastrectomy or distal subtotal gastrectomy at the N.N. Blokhin National Medical Research Center of Oncology in the period from 2005 to 2022. Distal localization of GC was identified as the tumor localized in the antrum of the stomach with or without spreading to the lower third of the stomach corpus. Such clinical and morphological factors as sex, age, tumor localization, depth of tumor invasion, macroscopic form of the tumor, number of affected lymphatic basins, lymphovascular or perineural invasion, and resection margins were identified and compared among the patient groups that were formed depending on the extent of the surgery performed. Pathomorphological staging was performed in accordance with TNM Classification of Malignant Tumors, 8th Edition.

Statistical Analysis. In the analysis of long-term outcomes, the relapse-free survival (RFS) was considered the period from the beginning of treatment to the emergence of signs of progression of the disease, death, or the last follow-up of the patient. The overall survival (OS) was considered the period from the beginning of treatment to all-cause death or the last follow-up. The statistical analysis included the Chi-square criterion used to test the hypotheses. Survival analysis was carried out by Kaplan-Meier method and compared by log-rank tests. The statistical analysis was carried out in the RStudio Version

Factors	DSG (N=87)	TG (N=38)	P
Age (years)			
<55	32 (36.8%)	23 (60.5%)	0.014
>55	55 (63.2%)	15 (39.5%)	
Sex			
M	35 (40.3%)	18 (47.4%)	0.0002
F	52 (59.7%)	20 (52.6%)	
Invasion depth			
T1 - T2	29 (33.3%)	14 (36.8%)	0.704
T3 - T4	58 (66.7%)	24 (63.2%)	
Borrmann type			
I - II	17 (19.5%)	5 (13.2%)	0.388
III - IV	70 (80.5%)	33 (86.8%)	
Lymph node status			
pN0	47 (54.0%)	22 (57.9%)	0.688
pN+	40 (46.0%)	16 (42.1%)	
Localization			
- antrum section			<0.001
- lower third of corpus and antrum section border	78 (89.7%)	21 (55.2%)	
- lower third of corpus and antrum section	7 (8.0%)	9 (23.7%)	
	2 (2.3%)	8 (21.1%)	
Stage			
IA/B	27 (31.0%)	11 (28.9%)	0.592
IIA/B	31 (35.6%)	15 (39.5%)	
IIIA/B/C	18 (20.7%)	10 (26.3%)	
IV	11 (12.7%)	2 (5.3%)	
Resection margin			
R0	81 (93.1%)	37 (97.4%)	0.340
R+	6 (6.9%)	1 (2.6%)	
Lymphovascular invasion			
Yes	6 (6.9%)	4 (10.5%)	0.491
No	81 (93.1%)	34 (89.5%)	
Perineural invasion			
Yes	4 (4.6%)	5 (13.2%)	0.088
No	83 (95.4%)	33 (86.8%)	
Relapse			
Yes	8 (9.2%)	1 (2.6%)	0.191
No	79 (90.8%)	37 (97.4%)	

Table 1. Clinical and morphological characteristics of patients depending on the surgical intervention performed

Таблица 1. Клинико-морфологические характеристики больных в зависимости от выполненного хирургического вмешательства

2023.09.0+463 software suite by Posit Software PBC. Two-sided significance levels of research used to test the hypotheses are 5%. Univariate and multivariate analysis between dependent and independent variables (determination of the independent influence of potential risk factors on the rate of occurrence of the studied event over the studied time period) was performed using the Cox proportional hazards (regression) model.

RESULTS

The following surgeries were performed to the following extents: total gastrectomy, 38 (30.4%); distal subtotal gastrectomy, 87 (69.6%). Of the 125 patients, 27 (21.6%) had early gastric cancer, 85 (68.0%) had locally advanced cancer, and 13 (10.4%), metastatic cancer. The age of patients was between 26 and 81 years (median age was 53.5 years). Tumor type according to P. Lauren in all patients was considered diffuse (100%). Among all patients, pN0, pN1, pN2 and pN3 was identified in 69 (55.2%), 23 (18.4%), 15 (12.0%) and 18 (14.4%) patients, respectively. Stages I, II, III, IV were identified in 38 (30.4%), 46 (36.8%), 28 (22.4%) and 13 (10.4%) patients, respectively. Patients with multiple primary tumors and neuroendocrine tumors were excluded from the study.

Correlation was studied between the extent of the surgery performed and age, sex, depth of tumor invasion, status of lymph nodes, Borrmann tumor classification, tumor staging, resection margin, presence of lymphovascular or perineural invasion, and incidence rate of intramural relapse of the disease. In our study, the group of patients who had undergone

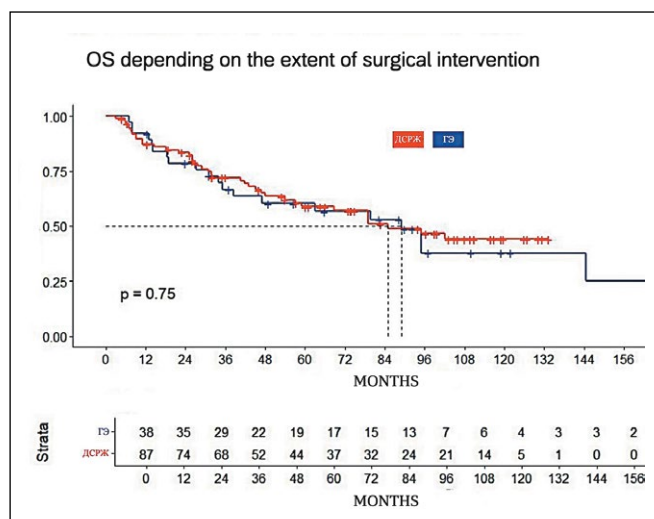


Figure 1. Overall survival depending on the extent of surgical intervention.

Рисунок 1. Общая выживаемость в зависимости от объема оперативного вмешательства.

DSG, had more females (59.7% vs. 52.6%; $p=0.0002$) and older persons (>55 years of age; 63.2% vs. 39.5%; $p=0.014$), than in the total gastrectomy group. It was also found that the tumor was more frequently localized only within the antrum section of the stomach in the DSG group vs. the TG group (89.7% vs. 55.2%; $p<0.001$). Perineural invasion had a tendency towards statistically significant difference between the two groups (4.6% vs. 13.2%; $p=0.088$). Other statistically significant differences were not identified. It is interesting to note that the patients of the DSG group had cancer cells along the resection margins more frequently (6.9% vs. 2.6%; $p=0.340$), and relapse was identified in them more often as well (9.2% vs. 2.6%; $p=0.191$). The data follows below in **Table 1**.

The median OS and 5-year survival in the DSG group were 85.0 months, 58.8% (95% CI: 0.487-0.711). The median OS and 5-year survival in the TG group were 89.0 months, 60.3% (95% CI: 0.460-0.791). The differences in overall survival are statistically unreliable ($p=0.75$) (**Fig 1**).

Univariate analysis was performed to assess the impact of clinical and morphological factors on overall survival. As shown in Table 1, the reliable prognostic value in the univariate analysis was in the depth of tumor invasion, status of affected lymph nodes, and stage of the tumor process. The margin of resection tended to be statistically significant on OS ($p=0.082$). The extent of the surgery performed had no impact on OS in the univariate analysis ($p=0.753$).

Next, a multivariate analysis was performed to determine the prognostic significance of clinical and morphological factors. Multivariate analysis revealed that only the stage of the tumor process had a statistically significant effect on OS. The results follow in **Table 2**.

In our study, only 84 (67.2%) patients showed up for follow-up at the N.N. Blokhin National Medical Research Center of Oncology after the surgery. Among the patients who showed up for the follow-up, 63 (75%) had undergone DSG, and 21 (25%), TG. In 89.3% (75/84) of the patients, no relapse of the disease was identified at the moment of the examination. In 10.7% (9/84) of the patients, relapse was identified: 7 patients (77.8%) with intramural recurrence in

the esophago- or gastro-enteroanastomosis, and 2 patients (22.2%) with intramural recurrence and distant metastasis. On average, the relapse of disease was identified 33 months after the surgery.

In the patients in the DSG group who showed for a follow-up, the intramural recurrence was identified in 12.7% cases of all relapses (8/63): in 6 patients, only the intramural recurrence in the gastro-enteroanastomosis was identified, and in two patients, the intramural recurrence and remote metastases. In 9% (7/78) of the patients in the DSG group with intramural recurrence, the primary tumor was initially localized within the antrum of the stomach. At the same time, only in two patients after the primary surgery (distal subtotal gastrectomy) positive resection margins were found along the stomach line (R1).

In the TG group, the patients who showed for the control follow-up, only one case (4.8%) of the intramural recurrence of the disease in the esophago-enteroanastomosis was identified, however, in this specific case the tumor was transferring from the antrum to the lower third of the stomach corpus. Of all the cases of the disease relapse, only two patients (25%) with intramural relapse were able to undergo repeated surgery. At the moment of the follow-up, six (66.7%) relapsing patients were dead from disease progression.

DISCUSSION

Diffuse gastric cancer according to P. Lauren, which includes the signet cell gastric cancer with characteristic morphology, had adverse prognosis, aggressive course, and resistance to chemotherapy [3-5, 16].

TG with D2 lymph node dissection is the preferred treatment approach for diffuse gastric cancer. However, it is related to lower quality of life of patients, unsatisfactory nutritive status and higher lethality as compared to DSG [12-14]. In the clinical recommendations of ESMO (2016), DSG was regarded as an alternative to the total gastrectomy for diffuse gastric cancer with at least 5 cm margin from the visual border of the proximal edge of the tumor [15].

The multi-center LOGICA study compared the immediate and long-terms results of surgical treatment of 211 patients with gastric cancer who had undergone total ($n=89$) or distal subtotal ($n=122$) gastrectomy with perioperative chemotherapy in the period from 2015 to 2018. The comparison of the two groups showed that diffuse tumors (51% vs. 31%; $p=0.005$) and lower rate of R0-resections (91% vs. 98%; $p=0.019$) were reliably more frequent in the TG rather than in the DSG group respectively. Positive resection margins in the TG group ($n=8$) in 88% of the cases were due to the diffuse type of the tumor. Both cases of positive resection margins in the DSG group were due to the diffuse type of the tumor. In the multivariate analysis, the diffuse type of the tumor is reliably associated with positive resection margins (RR 10.04; $p=0.035$). Also, in the DSG group lower rate of post-surgery complications was found (34% vs. 57%; $p<0.001$), such as leakage of anastomosis (3% vs. 19%), pneumonia (4% vs. 22%), atrial fibrillation (3% vs. 14%) as compared to the TG group ($p<0.05$). The overall survival showed a trend towards reliable difference ($p=0.084$). The only prognosis factor to affect overall survival was the neoadjuvant chemotherapy (RR 0.41; 95% CI: 0.20 – 0.87; $p=0.020$) [17].

The meta-analysis performed by J. Qi et al. (2016) compared patients depending on the surgery performed. The subgroup

Factor	Univariate analysis of OS		Multivariate analysis of OS	
	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)
Age (years)				
<55	1	1	-	-
>55	0.191	1.417 (0.841-2.387)	-	-
Sex				
M	1	1	-	-
F	0.115	0.660 (0.394-1.106)	-	-
Invasion depth				
T1	1	1	1	1
T2	0.144	2.171 (0.767-6.146)	0.673	1.303 (0.381-4.451)
T3	0.187	1.912 (0.730-5.009)	0.345	0.460 (0.092-2.308)
T4	0.002	3.240 (1.551-6.767)	0.363	0.456 (0.084-2.479)
Lymph node status				
N0	1	1	1	1
N1	0.265	1.559 (0.714-3.401)	0.338	0.527 (0.143-1.951)
N2	<0.001	3.818 (1.852-7.873)	0.942	1.056 (0.245-4.544)
N3	<0.001	5.394 (2.726-10.673)	0.973	1.027 (0.217-4.850)
Tumor stage				
IA/B	1	1	1	1
IIA/B	0.026	2.442 (1.113-5.359)	0.055	5.099 (0.968-26.858)
IIIA/B/C	<0.001	4.670 (2.061-10.580)	0.078	11.321 (0.762-168.153)
IV	<0.001	15.170 (6.084-37.826)	0.010	40.073 (2.380-674.606)
Borrmann type				
Type I	1	1	-	-
Type II	0.891	0.865 (0.108-6.898)	-	-
Type III	0.882	0.860 (0.117-6.318)	-	-
Type IV	0.785	1.371 (0.141-13.302)	-	-
Tumor localization				
- antrum section	1	1	-	-
- lower third of corpus and antrum section border	0.496	0.753 (0.333-1.703)	-	-
- lower third of corpus and antrum section	0.613	0.774 (0.287-2.088)	-	-
Resection margin				
R0	1	1	1	1
R1	0.082	2.280 (0.900-5.776)	0.313	1.745 (0.592-5.139)
Lymphovascular invasion				
Yes	1	1	-	-
No	0.677	1.216 (0.485-3.047)	-	-
Perineural invasion				
Yes	1	1	-	-
No	0.772	1.189 (0.369-3.829)	-	-
Preoperative chemotherapy				
No	1	1	-	-
Yes	0.586	0.723 (0.226-2.317)	-	-
Extent of surgery				
TG	1	1	-	-
DSG	0.753	0.915 (0.529-1.585)	-	-

Table 2. Results of uni- and multivariate analysis of the prognostic significance of clinical and morphological factors

Таблица 2. Результаты одно- и многофакторного анализа прогностической значимости клинико-морфологических факторов

analysis revealed that in the cases of total gastrectomy the incidence rate of intrabdominal apostasies was reliably higher (RR = 3.41; 95% CI: 1.21 – 9.63; $p < 0.05$). Five-year survival in the total and subtotal gastrectomy groups was 49.6% and 55.9% (RR = 0.91; 95% CI: 0.85 – 0.97; $p = 0.006$), respectively [18].

Performing distal subtotal gastrectomy in cases of distal diffuse gastric cancer may only be justified if the principles of radical surgery are respected and if there are no cancer cells along the resection margin (R0). S. Gaspar-Figueiredo et al. (2023) demonstrated in their study the negative influence of R1-resection on overall survival in cases of diffuse gastric cancer in 20 patients who had undergone total gastrectomy. The OS median in the patient group with R0N0 was 102 (95% CI: 1-207) months versus the groups with R1N+ and R1N0, where the OS median was 7 (95% CI: 1-13; $p < 0.001$) and 36 (95% CI: 13-59) months, respectively. Median RFS in the R0N0 group was 41 (95% CI: 32-50) months vs. R1N+ and R1N0 groups, where the median RFS was 4 (95% CI: 1-7) and 25 (95% CI: 17-33) months, respectively ($p < 0.001$). The multivariate analysis revealed that the resection margin was an independent factor for the adverse prognosis (RR 4.1; 95% CI: 3.4-12.3) [19].

M. Boubaddi et al. (2024) ran a retrospective multicenter analysis in which they compared two groups of patients with poorly cohesive gastric carcinoma: 140 patients (52%) underwent total gastrectomy and 129 (48%) underwent distal subtotal gastrectomy. The patients were similar in pTNM and major clinical characteristics. In terms of long-term outcomes of 5-year OS and RFS no reliable differences were found: in the TG group, 46% (95% CI: 35.9% – 55.5%); in the DSG group, 45.3% (95% CI: 34.3% – 55.6%). In the TG group, 5-year OS was 53.8% (95% CI: 43.2% – 63.3%); in the DSG group, 53% (95% CI: 41.4 – 63.3%) (RR 0.94; 95% CI: 0.68 – 1.29); 5-year RFS in the TG group was 46% (95% CI: 35.9% – 55.5%) vs. DSG group with 45.3% (95% CI: 34.3% – 55.6%) (RR 0.97; 95% CI: 0.70 – 1.34). The incidence rate of post-surgery complications according to Clavien-Dindo was reliably higher in the TG group in comparison with the DSG group ($p < 0.001$). At the same time, in the DSG group the positive resection margins (R1) were found more often than in the TG group (20.3% vs. 11.4%; $p = 0.046$). The factor analysis revealed that the R1-resection ($p = 0.08$) and the poorly cohesive morphological form with over 50% of signed-shaped cells ($p = 0.31$) do not reliably influence OS [20].

J.A. Gajardo et al. (2024) performed a retrospective analysis where two groups of patients with diffuse/mixed cancer according to P. Lauren: 62 patients underwent total gastrectomy (48%), and 68 underwent distal subtotal gastrectomy (52%). The distal cancer was identified as a tumor involving the lower third of the stomach corpus, or the antrum, or the pylorus. R0 resection was made in all of the patients. The post-surgery complication rate was similar in both groups (4.4% vs. 8.1%; $p=0.387$). The survival median in the TG group was 69 months, whereas in the DSG group, the median had not been reached ($p=0.097$); five-year OS in the TG group was 51%, and it was 63% in the DSG group. No reliable differences in RFS were found ($p=0.392$) [21]. M.A. Moslim et al. (2021) made a comparative study of 17,086 patients with gastric cancer. The study included patients with squamous cell carcinoma (SCC) and non-squamous cell carcinoma (non-SCC) who underwent DSG (25.5% vs. 20.9%) and TG (74.5% vs. 79.1%), respectively. The patients with SCC underwent TG more frequently ($p<0.001$). The patients in the SCC group, who had undergone distal subtotal gastrectomy, had better values of 5-year OS (RR = 0.67, 95% CI: 0.60-0.75; $p<0.0001$) [22].

In our study, we were able to demonstrate that the 5-year survival in the DSG group was comparable to that of the group of patients who had undergone total gastrectomy (58.8% and 60.3%, respectively). Such high values of OS are related to the fact that the examination of 67.2% identified stages I-II of the tumor process. The patients in the DSG group were reliably older than those in the TG group. The age and the presence of concomitant diseases may have a certain impact on the choice of the surgery, viz. choice of DSG to decrease risk of mortality. It is likely that it was in this regard that stomach resection was performed (87/125) rather than total gastrectomy.

It must be noted, though, that in the DSG group the incidence rate of R1-resections was somewhat higher than in the TG group (6.9% vs. 2.6%, respectively), which might be the cause for more frequent relapse cases in this group of patients. The univariate analysis revealed that the resection margin (R1) has a tendency towards a statistically significant

adverse impact on overall survival ($p=0.082$). In two out of eight patients with relapsing disease from the DSG group, the planned histological examination identified tumor cells along the proximal line of resection. Presence of tumor cells in the proximal margin of resection could have been an indication towards surgery before total gastrectomy in the event the same had been identified intraoperatively.

We were able to establish that during the follow-up the patients in the DSG group showed relapses of the disease in 12.7% of all relapse cases (8/63), and in seven patients of those the tumor was localized in the antrum of the stomach. In the group of patients who had undergone total gastrectomy, one case (4.8%) of intramural reoccurrence (1/21) was found, which, again, testifies to the aggressive biology of diffuse cancer and its potential towards development of intramural relapse in the esophago-enteroanastomosis area despite the surgical intervention. Notwithstanding the similar outcomes of overall survival between the two groups, the incidence rate of relapse is higher in the DSG group vs. the TG group. It may be concluded that in patients with distal localization of diffuse gastric cancer, total gastrectomy is the safer and more radical method of surgery, whereas distal subtotal gastrectomy is to be considered only in specific cases, where total gastrectomy entails high operative risk for the patient. Nevertheless, the choice of surgical intervention is to be carefully weighed.

CONCLUSION

Distal subtotal gastrectomy with D2 lymph node dissection in cases of distal gastric cancer does not have any reliable adverse effect on survival values ($p=0.75$). Performing the DSG for this category of patients entails higher risks of intramural recurrence of the disease in comparison with total gastrectomy, where the relapse risk is significantly lower.

Thus, today we cannot recommend DSG in distal diffuse gastric cancer as the alternative to the total gastrectomy, especially in the cases of the tumor transferring to the lower third of the stomach corpus due to higher incidence of intramural relapses. This may exclude patients of advanced age with manifested concomitant pathology. ■

ADDITIONAL INFORMATION	ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ
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Consent for publication. Written consent was obtained from the patient for the depersonalized publication of relevant medical information and all of accompanying images in the journal.	Информированное согласие на публикацию. Авторы получили письменное согласие пациента на публикацию в журнале медицинских данных и фотографий в обезличенной форме.
Contribution of individual authors. R.O. Torosyan – data collection, analysis and interpretation, preparation of the text of the article, determination of the patient's treatment tactics, planning and execution of surgical intervention. S.N. Nered, N.A. Kozlov, Sun H. – study concept and design, approval of the final version of the article. I.S. Stilidi. P.V. Kononets – editing of the article. All authors gave their final approval of the manuscript for submission, and agreed to be accountable for all aspects of the work, implying proper study and resolution of issues related to the accuracy or integrity of any part of the work.	Участие авторов. Р.О. Торосян – сбор, анализ и интерпретация данных, подготовка текста статьи. С.Н. Неред, Н.А. Козлов, Сунь Х. – концепция и дизайн работы, утверждение окончательного варианта статьи. И.С. Стилиди, П.В. Кононец – редактирование статьи. Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.

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