ANALYSIS OF SURVIVAL AFTER RADICAL SURGERY FOR STOMACH CANCER IN ODESSA REGIONAL CANCER CENTER

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ARTICLE INFO
Received 30 November 2017
Accepted 22 December 2017
Published 10 January 2018

KEYWORDS
stomach cancer,
lymphadenectomy,
survival

ABSTRACT
The survival of patients with the locally advanced stage of stomach cancer (SC), who underwent various variants of preventive lymphatic nodes dissection, was considered. The survival of patients was compared with the stage and T, N indexes. Lymphadenectomy D2 were effective and increased cumulative survival in patient`s group T4aNoMo, stage IIB and T4aN1Mo, stage III A, and in groups of patients where D2 lymphadenectomy were ineffective - T4bNoMo, stage IIIB, T4bN1Mo, stage IIIB and T4aN2Mo, stage IIIB. D2 were more efficient operation in the case of tumor serosa invasion and invasion to the peritoneal cavity (SE) in the absence of multiple metastases to the regional lymph nodes (N1 according to the 7th revision of the classification - 1-2 metastatic lymph nodes), and when the tumor infiltrated the surrounding organs (SI) and the presence of multiple regional metastases, D2 lymphodissection did not gave positive results, comparising with D1.

Extensive preventive removals of the surrounding lymph nodes (often completely healthy) affected by the tumor has long ceased to be a controversial issue in radical surgery of stomach cancer [1,3,9,11,13]. *"Onco- surgery is anatomy of the lymphatic system"*.

For staging purposes, classification of TNM is used, in which the stages attempt to reflect an objective criterion - the survival of patients with stomach cancer. Despite the constant changes, the classification stratifes the patients for different prognostic groups - stages [5,15].

Radical operative intervention depends on the volume of dissection of the lymph nodes. Three types of gastrectomies are distinguished, depending on the type of dissection. The implementation of standard gastrectomy means the removal of paragastric lymph nodes, which are located in the ligament apparatus of the stomach (Nos. 1-6); (level of lymphodissection-D1). Standard radical gastrectomy with limphatic D2 dissection means the simultaneous removal of groups of collectors Nos. 1-6, and the removal of retroperitoneal lymph nodes located along the celiac trunk (№ 9) and its branches - left gastric artery (№ 7), the common hepatic artery (№ 8), the splenic artery (№11) and the lymph nodes of the spleen gate (№ 10). And, finally, the term "extended radical" gastrectomy is applicable to the collectors of the hepatoduodenal ligament (№ 12), the retropancreatoduodenal nodes (№13), lymph nodes of superior mesenteric artery (№14), middle colic artery (№15), para-aortic lymph nodes located at the abdominal aorta level (№16) [1,3,11].

Approaches to the performance of D 2 and higher degrees of lymphatic dissection in stomach cancer have long been developed [3,13], however there are certain difficult questions that the oncologist's daily practice pays attention to. So, is there a need to perform D2 lymphodissection in case of complete tumor infiltration of stomach wall?

Lymph node dissection up to D2 level is defined as the standard of radical surgery for gastric cancer in the 4th International Surgical Congress of gastric cancer (2001, New York, USA) and at the 18th World Congress on Surgery of the gastrointestinal tract (2002 year, Hong Kong).

Identification of malignant cells in the peritoneal fluid is an independent predictor

factor. In patients without macroscopic signs of peritoneum dissemination in the case of the absence of such cells, the five- year survival rate was 49.3 %, with a positive response only 15.4 % [3]. With histologically confirmed involvment of the serous membrane of stomach or spreading to the surrounding organs, the five - year survival in the absence of peritoneal malignant cells in the abdominal cavity is 33.8 %, and when detected - only 8.3 % [3].

We analyzed the survival of such patients, there were performed preventive standard D2 dissections of the lymph nodes. The control group represented patients who underwent D1 and D1+ lymphatic dissections (optional removing of spleen).

A total of 188 patients operated on for gastric cancer in the period 2007-2011 were included in the study conducted on the basis of the abdominal oncosurgical department of the Odessa Regional Oncological Center. The study included only radical or conditionally radically operated patients. The average age is 60.6 ± 10.5 years, men - 120, women - 68.

Table 1. Distribution of patients with gastric cancer by age group

№	Age group	Number of patients
1.	30-39 years old	7
2.	40-49 years	21
3.	50-59 years	54
4.	60-69 years	63
5.	70-79 years	35
6.	80-90 years old	8
	Total:	188

A total of 126 gastrectomies and 62 distal subtotal resections were performed. Gastrectomy was performed according to Bondar methodic. Distal subtotal resections ended in most cases with the formation of gastroenteroanastomosis according to Billroth-2 in the modification of Hofmeister-Finsterer.

Table 2. Distribution of patients with gastric cancer by stages and volume of performed lymph node dissection

Stage and type of lymphodissection	Stages (TNM-7)				
	T4aNoMo 2B	T4aN1Mo 3A	T4bNoMo 3B	T4bN1Mo 3B	T4aN2Mo 3B
D1	16	10	20	8	16
D2	19	9	16	12	8
Total	35	19	36	20	24

The life expectancy of patients with cancer was studied. Information on longevity was obtained from the Regional Cancer Registry, and data were updated every 3 months. Further, survival tables were constructed for each group, stage and treatment method used. Survival was studied by constructing a regression model of proportional hazard intensities. D. Cox (1972) by the formula:

$$hi\,(t) = ho\,(t)\,x\,e\,b1X1 + b2X2 + b3X3 + ... + bnXp,$$

where h0 (t) - initial risk
b1 ... bn - regression coefficients
X1 ... X p - prognostic factors
When b = 0, the hazard ratio is 1.

Observations were censored: for those patients with whom they managed to maintain contact, censor = 0, but if the patient died, the censor was = 1. In the analysis of survival, the frequency of the event in time was studied - the median survival of patients, i.e. time for which the population of patients with cancer was halved. The starting point was the date of the operation, the time scale - the months of the patients' life, the event - the death of the patient.

The Regional Cancer Registry is an example of the so-called censored sampling. The sample, which must be mathematically analyzed, but which, due to objective and subjective reasons, does not contain complete information. The Kaplan-Mayer method, like the method of constructing survival tables and other methods, deals with censored samples. He has only one minus: he does not allow to assess the reliability of the differences between the two survival curves if they are crossed.

The right censorship was routinely taken into account - the patient's departure from surveillance, or death from other causes; and left excision - uneven inclusion of patients in the study (patients were included in the study in 2007, 2008, 2009, etc. years). In constructing the graphs, the Y-scale included the percentage of surviving S patients, and the X scale-the observation months. The advantage of the D.Cox model is that it is possible to add covariants, there is no need to correctly stratify the groups, have evidences of correctness of stratification.

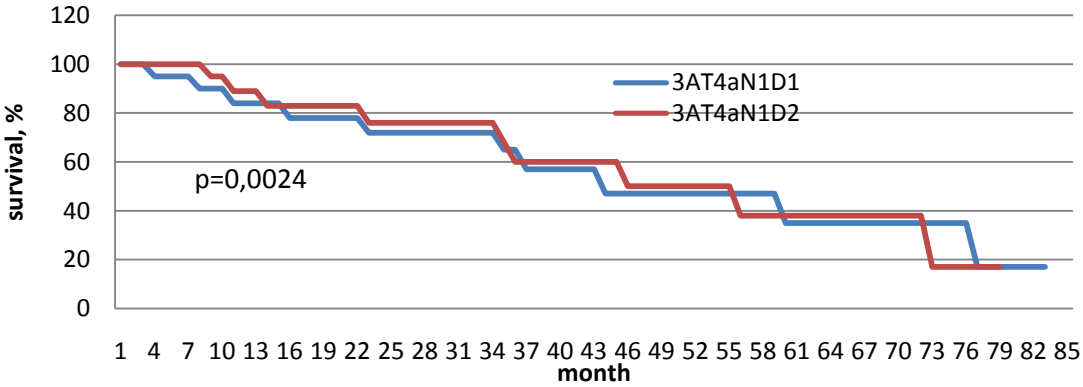

Fig. 1. Comparison of survival by calculation according to the Wilcoxon test p

Results of the study. In our model, patients with signs of entire stomach wall involvement were examined in accordance with the 7th revision of TNM classification. According to it, T4 is a situation where a tumor invades a serous membrane (and not just a subserosa as at T3) and (or) infiltrated surrounding organs. The category T4 divided into 2 subtypes: T4a and 4b, which may be more briefly discribed by two-letter abbreviations: abbreviation SE - involvement of serosa to the peritoneal cavity, SI - involvement of surrounding organs.

Visually, considering the obtained data, there is a survival gain at T4aNo for the D2 group of dissection of lymph nodes in the interval of 3-6-9-12-24-36 months. After 48 months, D2 dissection of the lymph nodes does not give an increase in life expectancy. Three-year and five-year survival rates in the group were quite high and amounted to D1 and D2 radical operations 57, 67, 46 and 43 % respectively, which is undoubtedly high in surgery of the locally advanced stage in stomach cancer. For both groups of T4aN1, the superiority of more extensive dissections affected the timing of 3 to 72 months. For group T4bNo removing of more lymph nodes was not effective. The same situation was observed in the T4bN1 group - life expectancy (until it is "survival", the cumulative index, namely the arithmetic sum of months of life) after standard operations was higher than after standard radical (D1> D2). And only after 72 months of observation the situation changed. T4bN3: only in the period from 3 to 12 months, the standard radical surgery (Nos. 7-10) gave a preponderance over the removal of paragastral groups of lymph nodes (Nos. 1-6).

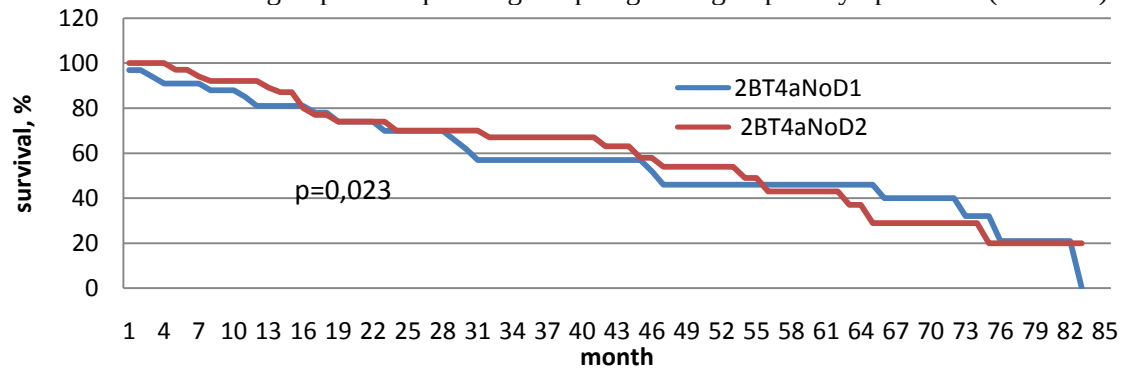

Fig. 2. Survival of gastric cancer patients in 2B stage: T4aNo

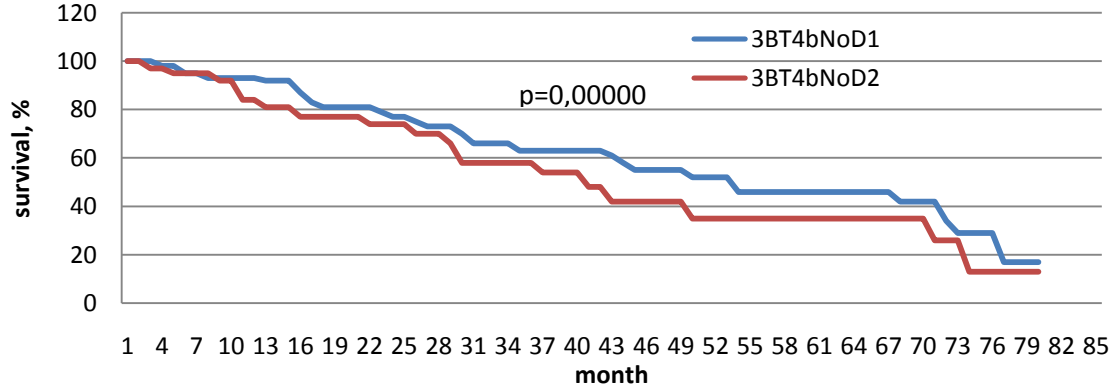

Fig. 3. Survival of gastric cancer patients in 3B stage: T4bNo

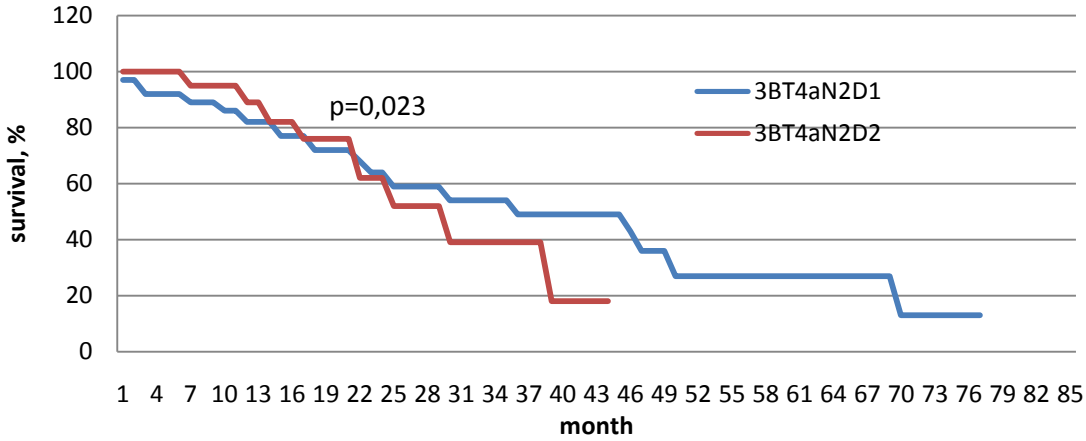

Fig. 4. Survival of gastric cancer patients in 3B stage: T4aN2

It is concluded that a broader removal of lymphatic collectors does not change the survival of patients with gastric cancer when the tumor grows into neighboring structures, for example, a large omentum; while a simple invasion of the serous membrane by the tumor is not a contraindication to the implementation of extended lymphodissection with locally advanced forms of stomach cancer.

Let me once again list the values of p differences in the survival between D1 and D2 dissections.

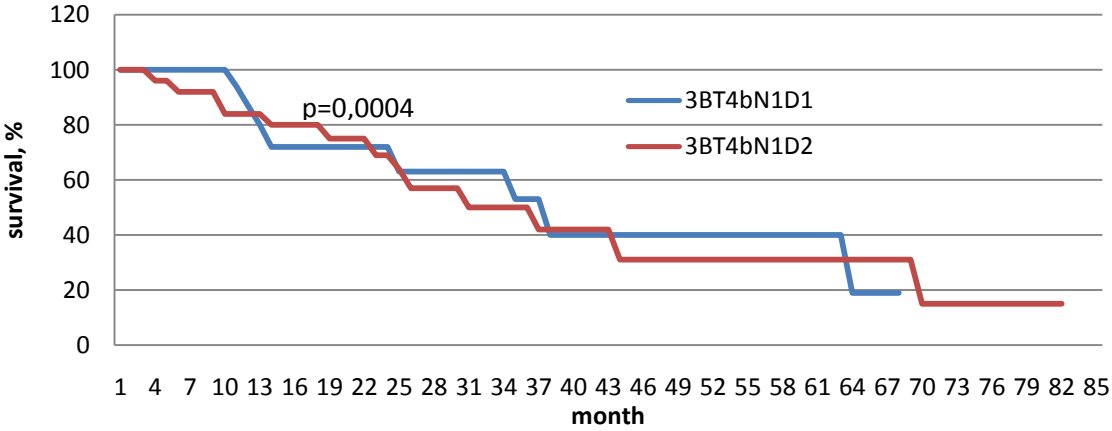

Fig. 5. Survival of gastric cancer patients in 3B stage: T4bN1

Table 3. Data of reliability of differences between groups of calculations.

Group of patients	D	R
T4aNo 2B	D1	0.023
	D2	
T4aN1 3A	D1	0,0024
	D2	
T4bNo 3 B	**D1**	**0.000 ... .0042**
	D2	
T4bN1 3 B	D1	0.0004
	D2	
T4aN2 3B	D1	0.023
	D2	

At the 4th International Congress of gastric cancer (2001, New York) performing of D2 lymph dissections for gastric cancer is defined as a standard component of radical surgery for tumors of stage T_3-T_4, in the absence of hematogenous metastases. Our research in any case does not call into question the appropriateness of this type of operations. Research interest was whether results can differ from the standard approaches. Interestingly, the increase in the number of lymph nodes removed during surgery by itself may affect the accuracy of staging stomach cancer. There is a significant difference between 5th, 6th and 7th types of classification in counting the number of affected lymph nodes. For example, in the 4th and 5th editions paragastric metastases characterized as N1, those located along the branches of the celiac trunk - as N2, paraaortic and retropancreatic - as N3. At the same time, 6th and 7th edition classification only require to carry out mathematical calculation found metastases. The 6th edition: N1 means affected 1-6 lymph nodes, N2 – in 7-15 found regional metastases, N3 - more than 16 lymph nodes. Thus, the 6th revision of the classification makes

surgeon removes at least 16 lymph nodes, as otherwise the staging will be incorrect.

6th revision contributed to the great surgical outcome in the direction of implementation of more and more careful lymphadenectomy. In most "advanced" hospitals after surgery performed not only counting the number of lymph nodes removed, but classification in special groups of Japanese classification [5].

Needless to say, the seventh classification does not give up, but rather continues the above tradition. Now N divided by not only 3 but 4 groups: N1, N2, N 3a, N 3b. Where N1 - 1-2 affected lymph nodes, N2 - 3-6 affected lymph nodes, N3a 7-15 lymph nodes, N3b - more than 16. Thus, "magic" number 16 in this case is stored, and if the surgeon during surgery removes at least 15 lymph nodes, any further discussion on the correct staging is in the past.

Conclusions. Infiltration of the stomach wall and adjacent structures involvment - signs of adverse prognosis in gastric cancer.

D2 lymphadenectomy have been considered as effective and increasing the cumulative survival of patients procedure in 2A, 2B, 3A stages; groups wherein D2 were ineffective in our research - 3B stage.

Further radicalisation of surgical procedure by performing more extensive prophylactic dissection of an increasing number of lymph nodes does not increase survival in some specific groups of these patients (SE+/SI+).

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