

## THE EFFECT OF ENDOSCOPIC AND INTRAOPERATIVE RESULTS ON THE TYPE AND EXTENSIVENESS OF STOMACH CANCER OPERATION

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Gastroscopy is the main method for diagnosing malignant disease of the stomach.

The aim of the paper was to prove that endoscopic results together with intraoperative finding determine the type and extensiveness of the cancer operation.

The study included 70 patients, all of them with the diagnosis of cancer or adenocarcinoma of the stomach, using the method of gastroscopy and pathohistological (PH) verification. Of this number, 38 patients underwent radical operation (total or subtotal gastrectomy) with systemic lymphadenectomy; 15 patients underwent palliative operation for improving the quality of life; 15 patients underwent explorative laparotomy for making the final diagnosis and possible palliative operation; 2 patients died due to poor general medical condition of the organism after making the endoscopic and pathohistological diagnosis. The obtained data were processed and presented in tables and charts. In all applied analytical methods, the level of significance was 0,05.

The treatment outcome did not depend on the localization (regio antri et pylori, regio cardiae, regio pangastrica, regio corporisi) and macroscopic finding of the tumor (ulceroinfiltrative, diffuse infiltrative, ulcerative, fungoid form). Worse TNM status, worse P and H classification in the patients before the applied therapy significantly influenced the survival rate. Similar findings were also confirmed for the definitive TNM status, P and H classification. The treatment outcome was significantly influenced by the pH finding, as intestinal type of cancer prevailed in the deceased. Prognostically, the presence of metastases had the worst influence on the course and outcome of the treatment.

Early diagnosis of stomach cancer is of greatest importance for survival of these patients. Tumor size (T), the pathohistological result (PH) and lymphonodal status (N) significantly influence the extent of radical operative treatment and distant metastases. By applying radical lymphadenectomy with total and subtotal gastrectomy, survival length increases, which we expect in our patients whose health is constantly being monitored; they are in a good general medical condition, with no signs of relapse. By applying radical extensive lymphadenectomy, the rate of survival is increased. *Acta Medica Medianae* 2008;47(3):44-50.

**Key words:** gastroscopy, edoscopy, carcinoma ventriculi

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### Introduction

#### Treatment of stomach malign illnesses (cancers)

So far, surgical treatment has been the only known way for treating stomach cancer successfully (1,2,3,4).

As far as surgical therapy in stomach cancer treatment is concerned, differentiation between terms resectability and operability should be made.

The term *resectability* implies that the technical act is justified only if there are no distant metastases.

*Operability*, as a term, refers to a biological development of a malign tumor.

It means that a tumor with distant metastases is biologically inoperable but it can be technically resectable. In other words, a tumor can be operable because there are no distant metastases but its resectability can be at stake in cases where tumor has spread on the adjacent organs and blood vessels.

Clinical signs of inoperability are: supraclavicular adenopathy, clearly palpable tumor mass, signs of ascites and palpable liver nodes.

Intraoperative signs of inoperability are: tumorous infiltration of adjacent organs and blood vessels, distant metastases (in liver), carcinoma of peritoneum and ascites. Metastases

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in regional lymph nodes do not necessarily mean inoperability because radical operation always includes systemic lymphadenectomy.

Contemporary operative technique is based on two principles (5,6):

- removal of lesion where the borders of resection must be within healthy tissue (resection in healthy tissue) and
- removal of all regional lymph nodes (systemic lymphadenectomy).

In intestinal type of carcinoma, resection borders must be in oral direction at least 5 cm set away from a microscopically visible tumor borders. In diffuse type of carcinoma, resection border is set orally 10 cm from the visible tumor border. Radical surgical treatment includes total and subtotal gastrectomy with D2 lymphadenectomy (7,8).

Radical surgery implies the removal of omentum, total gastrectomy, splenectomy and systemic lymphadenectomy (suprapylorus, infrapylorus, epiploic, celiac, cardiac, retropancreatic and a group of nodes around liver hilus). Reconstruction is done according to "omega" type, which means termino-lateral esophagojejunum anastomosis with obligatory jejunojunction anastomosis. However, nowadays, doctors mostly do reconstruction with isolated jejunal circumvolution (Roux) using a mechanical joint (stapler) (9,10,11).

Subtotal resection has indications only in older persons or in cases of superficial carcinoma (early cancer) localized in the prepilorus region with no signs of metastatic changes in celiac and cardiac group of lymph nodes, verified *ex tempore* during the operation (8,9,10).

Gastroenteroanastomosis, as one of the types of palliative surgery, enables stomach functions.

Therapy of metastases in the liver in terms of resection is logical in cases when a metastatic change is solitary or if the target of a change is only in one lobe. Good results can be achieved also by embolisation using catheterisation and injecting cytostatics 5-Fluorouracil or a combination of three cytostatics. (5-Fluorouracil, Adriamycin i Mitomycin C), as well as injecting nitrosourea preparations. Monocytostatic therapy has approximately 20% of partial remissions and using, for example, FAM protocol (5-Fluorouracil+Adriamycin +Mitomycin C) we can reach an answer of 40%. However, it is necessary to say that remissions which occur are of relatively short duration and that cytostatic therapy at stomach carcinoma does not give good results (9,10,12).

### Aims

1. To prove that endoscopic results with intraoperative findings determine the type and extensiveness of an operation in case of carcinoma.

### Material and methods

This study included 70 patients, all of them with the diagnosis of cancer or adenocarcinoma

of the stomach, using the method of gastroscopy and a pathohistological (PH) verification. From this group, 38 patients underwent radical operation (total or subtotal gastrectomy) with a systemic lymphadenectomy, 15 patients underwent palliative operation for improving the quality of life, 15 patients underwent explorative laparotomy for establishing the final diagnosis and eventual palliative operation, 2 patients died due to poor general medical state of the organism after endoscopic and pathohistological diagnoses had been made.

The data are retrospective-prospective, gathered in a MC Cacak in Cacak, for the period 2003 – 2006.

The data have held a diagnostic standard for a stomach carcinoma which includes: medical history, clinical examination, laboratory results (blood picture: HGB, HCT, MCV, Fe), radiography of the stomach, gastroscopy with the stomach biopsy and pathohistological verification (PH), digitorectal examination (cul de sac phenomenon), X-ray of heart, lungs and bone system.

Apart from basic diagnostic procedures, the following ones were also performed:

- ~ Endosonography of the stomach
- ~ Ultrasound of the abdomen, if necessary
- ~ a scanner (CT) of the abdomen with a contrast
- ~ Scintigraphy of the liver
- ~ Tumor markers (CA-50, CA-19-9)
- ~ Immunological status
- ~ Laparoscopy
- ~ Explorative laparotomy

### Questionnaire for malignant illnesses

Questionnaire was based on standard and non-standard procedures during diagnosis of patients with gastric cancer (2,3,5,13).

- Name and surname
- Gender
- Age
- Address
- Gastroscopy
- Staging of disease (stage before the operation – used TNM classification) (stage after the operation)
- Histological type of tumor:
  - Diffuse
  - Intestinal
  - Undetermined
- Macroscopic view of a tumor:
  - Fungoid form
  - Ulcerous form
  - Ulcero-infiltrative form
  - Diffuse-infiltrative form
- Lymphonodal status
- Type of operation :
  - Radical operation
  - Palliative operation
  - Explorative operation
- Type of resection:
  - Total gastrectomy
  - Subtotal gastrectomy
- Outcome :
  - Alive
  - Passed away

**TNM classification (4,14)**

- **T1**– invasion of a tumor into the mucosa or submucosa **T2** – invasion of a tumor in m. propria or subserosus layer, **T3** – penetration of tumor into the serosa, **T4** – invasion of tumor into the adjacent structures.
  - **N0**- no evidence of metastases of lymph node; **N1** - metastases up to a group 1 lymph nodes, but none up to groups 2, 3 and 4; **N2** - metastases up to a group 2 lymph nodes, but none up to a lymph nodes 3 and 4; **N3** - metastases up to a group 3 lymph nodes, but without metastases up to lymph nodes of group 4; **N4** - metastases in lymph nodes of group 4.
  - **P0**- no peritoneal metastases; **P1** - metastases up to nearby peritoneum but not to a distant peritoneum; **P2** – a few metastases up to a distant peritoneum; **P3** - numerous metastases up to a distant peritoneum. Nearby peritoneum: Peritoneum of a smaller bag and a smaller and bigger omentum.
  - **H0**– no sign of liver metastases; **H1** - metastases limited to a single lobus, **H1 (dex)** -metastases limited to the right lobus, **H1 (sin)** - metastases limited to the left lobus; **H2** – a few metastases in both lobuses; **H3** - numerous metastases in both lobuses.
  - **M0**– no signs of distant metastases except peritoneal or liver metastases.
  - **M1**- distant metastases except for peritoneal or liver metastases.
- Category **M1** should be specified under the following marks:
- Brain (BRA), Bone marrow (MAR), Meninges (MEN), Bone (OSS), Pleura (PLE), Pulmonary (PUL), Skin (SKI), Pleura (PLE), Other (OTH).**

**Statistic methodology**

Received data are processed and shown in the tables and charts together with an appropriate discussion on the subject and all depending on nature of the stated variable.

Descriptions of numerical marks in our study are made by classic methods of descriptive statistics using arithmetical average values, and also by median of average values, and of variability measures by standard deviation, coefficient of variation and standard error, as well as by using minimal and maximal values. Relative numbers are used in all tables.

In our analyses, depending of the nature of variables, we used Pearson's chi- square test, in the form of matching tests and contingency tables, for comparing differences between frequencies in non-parametric features. In numerical limitations of a table two by two, we used the Fischer's test of exact probability.

For comparison of the Student's test for two groups of data. As a non-parametric addition to independent samples, we used a summary-

range test, and to dependant samples we used a test of equivalent pairs.

In comparison of three or more groups of data, we used Fischer's parametric analysis of variance (ANOVA) in parametric data, and non-parametric analysis of variance for a proportion in non-parametric data.

In an analysis of association, methods of single or multiple correlation and regression were used.

For the analysis of survival predicting and for development of hypertension, we used Cox's proportional hazardous method and logistic regression invariant in control with Log rank test for a comparisons between groups.

All applied analytical methods have shown a level of significance 0.05.

For creation of database and processing of data, a program named "Institute", made by Department for medical statistics and computer science at the Faculty of Medicine, University of Belgrade was used.

**Results**

Table 1 shows the frequency of tumor localisation in regard to the treatment outcome.

Table 1. Frequency of tumor localisation in regard to treatment outcome

		Tumor localizations				Total
		regio antri et pylori	regio cardiae	regio pangastrica	regio corporis	
Outcome	Alive	12	5	1	8	26
	Passed away	18	6	9	11	44
Total		30	11	10	19	70

The analysis of tumor localisation frequency in regard to the treatment outcome showed that there was no statistically significant difference ( $F=3,786$ ;  $df=3$ ;  $p>0,05$ ), which was the result of having all localizations relatively regularly arranged in both outcomes.

Table 2 shows the frequency of macroscopic tumor findings in regard to the treatment outcome.

Table 2. Frequency of macroscopic tumor findings in regard to the treatment outcome

		Macroscopic finding				Total
		ulcero infiltrative	diffuse-infiltrative	ulcerative	fungoidal form	
Outcome	Alive	9	12	4	1	26
	Passed away	22	16	3	3	44
Total		31	28	7	4	70

The analysis of frequency of macroscopic tumor findings regarding the treatment outcome showed that there was no statistically significant

difference ( $F=2,717$ ;  $df=3$ ;  $p>0,05$ ), which was the result of the fact that both outcomes were equally distributed.

Table 3 shows the frequency of carcinoma metastases in regard to the treatment outcome.

Table 3. Frequency of carcinoma metastases in regard to the treatment outcome

		Metastases		Total
		Developing	Not developing	
Outcome	Alive	7	19	26
	Passed away	3	41	44
Total		10	60	70

The analysis of frequency of carcinoma metastases in regard to the treatment outcome showed that there was high statistically significant difference ( $\chi^2=5,395$ ;  $df=1$ ;  $p<0,01$ ), which was the result of having a smaller number of metastases developing in the patients who survived than in the patients who passed away (ratio of metastases occurrence was 73.0 to 93.2%).

Table 4 shows the frequency of T classification before the therapy in respect to the treatment outcome.

Table 4. Frequency of T classification before the therapy in respect to the treatment outcome

		T before TH				Total
		T1	T2	T3	T4	
Outcome	Alive	2	4	16	4	26
	Passed away	0	3	14	21	38
Total		2	7	30	25	64

The analysis of the frequency of T classification before the therapy shows that there was high statistically significant difference ( $F=9,108$ ;  $df=3$ ;  $p<0,01$ ), and this is the result of the fact that the patients with T3 stage were more frequent in the survived, whereas the passed away were mostly in T4 stage (ratio is 61.5 to 55.3%).

Table 5 shows the frequency of N classification before the therapy in respect to the treatment outcome.

Table 5. The frequency of N classification before the therapy in respect to the treatment outcome

		N before TH					Total
		N0	N1	N2	N3	N4	
Outcome	Alive	7	16	2	1	0	26
	Passed away	4	11	7	17	1	38
Total		11	27	9	18	1	64

The analysis of frequency of N classification in respect to the treatment outcome shows that there was high statistically significant difference

( $F=17, 565$ ;  $df=3$ ;  $p<0,01$ ), which is the result of the survived mostly being in a N1 stage whereas the passed away mostly being in N2 and N3 (ratio is 61.5 to 60.0%).

Table 6 shows the frequency of P classification before the therapy in respect to the treatment outcome.

Table 6. The frequency of P classification before the therapy in respect to the treatment outcome

		P before TH			Total
		T1	T2	T3	
Outcome	Alive	26	0	0	26
	Passed away	25	1	14	40
Total		51	1	14	66

The analysis of the frequency of P classification before the therapy shows that there was high statistically significant difference ( $F=12,618$ ;  $df=2$ ;  $p<0,01$ ), which was the result of the survived mostly being in P0 stage whereas the passed away mostly being in P3 (ratio for P3 is 0.0 to 35.0%).

Table 7 shows the frequency of H classification before the therapy in respect to the treatment outcome.

Table 7. The frequency of H classification before the therapy in respect to the treatment outcome.

		H before TH			Total
		H0	H1	H3	
Outcome	Alive	26	0	0	26
	Passed away	26	3	11	40
Total		52	3	11	66

The analysis of the frequency of H classification before the therapy in respect to the treatment outcome showed that there was high statistically significant difference ( $F=11,550$ ;  $df=3$ ;  $p<0,01$ ), which was the result of the survived mostly being in a H0 stage, whereas the passed away mostly being in H3 (ratio for H3 is 0.0 to 27.5%).

Table 8 shows the frequency of our patients regarding the outcome of the treatment and M classification before the therapy.

Table 8. The frequency of our patients regarding the outcome of the treatment and M classification before the therapy

		M before TH			Total
		M0	M1	M2	
Outcome	Alive	23	1	2	26
	Passed away	30	9	1	40
Total		53	10	3	66

The analysis of frequency of our patients regarding the outcome of the treatment and M

classification before the therapy shows that there was no statistically significant difference ( $F=4,909$ ;  $df=3$ ;  $p>0,05$ ), which was the result of having stages of M classification relatively equally distributed in both the survived and the deceased groups.

Table 9 shows the frequency of pH tumor findings in respect to the treatment outcome.

Table 9. The frequency of pH tumor findings in respect to the treatment outcome

		PH		Total
		intestinal	diffuse	
Outcome	Alive	12	13	25
	Passed away	30	13	43
Total		42	26	68

The analysis of the frequency of the pH tumor finding in respect to the treatment outcome showed that there was high statistically significant difference ( $\chi^2=3,772$ ;  $df=1$ ;  $p<0,05$ ), which was the result of the survived having evenly present both pH variants, whereas the intestinal type was dominant in the deceased (ratio for intestinal 70.0 to 48.0%).

Table 10 shows the frequency of definite T tumor classification in respect to the treatment outcome.

Table 10. The frequency of definite T tumor classification in respect to the treatment outcome

		T before TH				Total
		T1	T2	T3	T4	
Outcome	Alive	24	1	1	0	26
	Passed away	14	2	4	20	40
Total		38	3	5	20	66

The analysis of the frequency of T tumor classification in respect to the treatment outcome showed that there was high statistically significant difference ( $F=22,822$ ;  $df=3$ ;  $p<0,01$ ), which was the result of the survived being mostly in T0 stage, whereas T4 prevailed in the deceased (ratio for T4 is 0.0 to 50.0%).

Table 11 shows the frequency of definite N tumor classification in respect to the treatment outcome

Table 11. The frequency of definite N tumor classification in respect to the treatment outcome

		Definite N				Total
		N0	N1	N2	N3	
Outcome	Alive	23	3	0	0	26
	Passed away	14	4	5	1	40
Total		37	7	5	1	66

The analysis of the frequency of definite N tumor classification in respect to the treatment outcome showed high statistically significant difference ( $F=22,369$ ;  $df=4$ ;  $p<0,01$ ), which was the result of the survived being mostly in N0 stage, whereas N3 was dominant in the deceased (ratio for N0 is 88.5 to 35.0%).

Table 12 shows the frequency of definite P tumor classification in respect the treatment outcome.

Table 12. The frequency of definite P tumor classification in respect the treatment outcome

		Definite P			Total
		P0	P1	P3	
Outcome	Alive	26	0	0	26
	Passed away	25	2	13	40
Total		51	2	13	66

The analysis of the frequency of P tumor classification in respect to the treatment outcome showed that there was high statistically significant difference ( $F=12,618$ ;  $df=2$ ;  $p<0,01$ ), which was the result of the survived being mostly in P0 stage, whereas P3 was dominant in the deceased (ratio for P0 is 100.0 to 65.0%).

Table 13 shows the frequency of definite H tumor classification in respect the treatment outcome.

Table 13. The frequency of definite H tumor classification in respect the treatment outcome

		Definite H			Total
		H0	H1	H3	
Outcome	Alive	26	0	0	26
	Passed away	26	2	12	40
Total		52	2	12	66

The analysis of the definite H classification frequency in respect to the treatment outcome showed that there was high statistically significant difference ( $F=11,550$ ;  $df=2$ ;  $p<0,01$ ), which was the result of the survived being mostly in H0 stage, whereas H3 was dominant in the deceased (ratio for H0 is 100.0 to 65.0%).

Table 14 shows the frequency of definite M tumor classification in respect to the treatment outcome.

Table 14. The frequency of definite M tumor classification in respect to the treatment outcome

		Definite M			Total
		M0	M1	M2	
Outcome	Alive	25	0	1	26
	Passed away	32	6	2	40
Total		57	6	3	66

The analysis of M tumor classification frequency before the therapy showed that there was no high statistically significant difference ( $F=4,442$ ;  $df=2$ ;  $p>0,05$ ), which was the result of having the stages of M classification relatively evenly distributed in both the survived and the deceased, with the domination of M0.

Table 15 shows the frequency of the operation type applied in the treatment of tumor in respect to the treatment outcome.

Table 15. The frequency of the operation type applied in the treatment of tumor in respect to the treatment outcome.

		Operation			Total
		palliative	explorative laparotomy	radical	
Outcome	Alive	1	0	25	26
	Passed away	14	15	13	42
Total		15	15	38	68

The analysis of the frequency of the operation type applied in the treatment of tumor in respect to the treatment outcome showed that there was high statistically significant difference ( $F=27,832$ ;  $df=2$ ;  $p<0,01$ ), which was the result of the fact that the survived mostly underwent radical surgeries and the deceased mostly underwent palliative operations and explorative laparotomy (ratio for radical surgeries is 96.2 to 30.9%).

## Discussion

The analysis of the frequency of our patients regarding the outcome of the treatment and tumor localization as well as macroscopic results shows that there is no statistically significant difference, which is the result of the fact that all localizations and macroscopic results were relatively equally distributed.

The analysis of frequency of our patients regarding the outcome of the treatment and metastatic findings shows that there was high statistically significant difference, which is the result of having a smaller number of metastases developing in the patients who survived than in those who passed away (ratio of metastases occurrence was 73.0 to 93.2%).

The analysis of frequency of our patients regarding the outcome of the treatment and the type of the operation of the tumor shows that there is high statistically significant difference, which is the result of the fact that the survived mostly underwent radical surgeries and the deceased mostly underwent palliative operations and explorative laparotomy (ratio for radical surgeries is 96.2 to 30.9%).

The data presented here confirm that the best organized services (Japan) detect early stomach cancer in 30% of the cases, whereas European health services detect stomach cancer mostly in 10% of the cases, which means that the patients usually come with a malignant stomach carcinoma in an advanced stage. With earlier developmental stage of carcinoma (smaller extent of an infected stomach tissue, smaller percentage of the infected lymph nodes, no metastases) there is greater possibility for radical cure (2,3,4,5). On the contrary, there are some situations such as clinical signs of inoperability: supraclavicular adenopathy, clearly palpable tumor mass, signs of ascites and palpable liver nodes, as well as intraoperative signs of inoperability: tumorous infiltration of nearby organs and blood vessels, distant metastases - in liver, carcinoma of peritoneum and ascites) when it is possible to perform only palliative and explorative surgery (2,4,9,10,15).

## Conclusions

Early diagnostics of stomach cancer has the greatest importance for the survival of these patients.

Size of a tumor (T), pathohistological result (PH), and lymphonodal status (N) have great impact on the extent of radical operative treatment and distant metastases.

By applying radical lymphadenectomy with a total and subtotal gastrectomy, the duration of survival increases. This is the case with our patients who are constantly monitored and are in good general medical condition with no signs of relapse.

The use of radical extensive lymphadenectomy increases the rate of survival.

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## UTICAJ ENDOSKOPSKOG I INTRAOPERATIVNOG NALAZA NA VRSTU I OPSEŽNOST OPERACIJE KARCINOMA ŽELUCA

Aleksandra Ž. Krstić

Gastroskopija je glavna metoda za dijagnostiku malignih oboljenja želuca.

Cilj rada bio je da se dokaže da endoskopski nalaz uz intraoperativni nalaz utvrđuje vrstu i opsežnost operacije kod karcinoma.

U ovom radu je obrađivano 70 bolesnika, od kojih su svi imali dijagnostikovani karcinom ili adenokarcinom želuca, putem gastroskopije i sa patohistološkom (PH) verifikacijom. Od toga, 38 bolesnika je operisano radikalnom operacijom (totalnom ili subtotalnom gastrektomijom) sa sistemskom limfadenektomijom, kod 15 bolesnika je urađena paliјativna operacija radi poboljšanja kvaliteta života a kod 15 bolesnika je urađena eksplorativna laparotomija radi postavljanja konačne dijagnoze i eventualne paliјativne operacije, a dva bolesnika su umrli usled lošeg opšteg zdravstvenog stanja nakon postavljanja endoskopske i patohistološke dijagnoze. U svim primenjenim analitičkim metodama nivo značajnosti bio je 0,05.

Ishod lečenja nije zavisio od lokalizacije (regio antri et pylori, regio cardiae, regio pangastrica, regio corporisi) i makroskopskog nalaza (ulcero infiltrativni, difuzno infiltrativni, ulcerativni, fungoidna forma) tumora. Lošiji TNM status, lošija P i H klasifikacija kod bolesnika pre primenjene terapije imaju značajan uticaj na stopu preživljavanja bolesnika. Slični nalazi su potvrđeni i za definitivni TNM status, P i H klasifikaciju. Ishod lečenja je značajno zavisio od ph nalaza tumora, jer je kod umrlih bolesnika preovladavao intestinalni tip karcinoma. Prisustvo metastaza imalo je prognostički najnepovoljniji uticaj na tok i ishod oboljenja.

Rana dijagnostika karcinoma želuca je od najveće važnosti za povoljan ishod u preživljavanju ovih pacijenata. Veličina tumora (T), kao i patohistološki nalaz (PH), limfonodalni status (N) značajno utiču na radikalnost operativnog lečenja i udaljene metastaze. Primenom radikalne limfadenektomije sa totalnom i subtotalnom gastrektomijom povećava se dužina preživljavanja, što očekujemo kod naših bolesnika koje i dalje pratimo a oni su u dobrom opštem stanju bez znakova recidiva. Primenom radikalne ekstenzivne limfadenektomije povećava se stopa preživljavanja. *Acta Medica Medianae* 2008;47(3):44-50.

**Ključne rači:** gastroskopija, edoskopija, karcinom želuca, TNM status