PATOHISTOLOGICAL FINDING IN GASTRIC CANCER DIAGNOSIS

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The paper presents the investigation involving 70 patients with gastric cancer diagnosis pathohistologically verified. The aim of the paper was to establish the importance of gastroscopy as a reliable method for gastric cancer diagnosis as well as the importance of patohistological result (PH) for the localisation, and macroscopic result of the cancer and the outcome and survival time in these patients. The data are retrospective-prospective. The conclusions, besides the confirmation of the importance of gastroscopy, also represent the fact that intestinal cancer type has slower development and better prognosis – five-yaer survival rate in 62%, while diffuse type metastasizes through lymphatic system with five-year survival rate in 5% in comparison to the early cancer in 92%. *Acta Medica Medianae 2009;48(3):*15-19.

Key words*: gastrscopy, gastric cancer, pathohistological result*

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INTRODUCTION

Gastric cancer is one of the most frequent malignant neoplasms of the gastrointestinal tract. It is rarely diagnosed in the population under the age of 30; about 10% of patients are under the age of 50; the mean age of the patients is between 55 and 65 years. Males are more affected than females, in ration 2:1 (1).

Gastroscopy – malignant lesion looks like irregular ulcerous lesion whose bottom appears brownish during endoscopic examination; the edges are sapped and irregular, the adjacent tissue is with pseudopolipoidal infiltration, while mucous membrane is inflexible.

Macroscopic classification of advanced gastric cancer

Nowadays, in numerous modern publications, Bormann's classification is still in use. It is simple, has only four main forms, as Ottenjan and Classen (1-3) state, and it is still used in endoscopy:
I.   Fungal form
II. Ulcerous form
III. Ulcerous-infiltrative form
IV. Diffuse-infiltrative form

Microscopic classification of advanced gastric cancer

In modern literature, a generally accepted definition is often used, and that is the Lauren's one. Lauren's simple classification (4) has been accepted for determination of main histo-morphological types of gastric cancer by most pathologists. It was based on the material taken from about 1500 gastric cancer gastrectomies, collected for ten years. The tumor's look, mucous secretion, histology as well as cancer citology are the main parametres of his classification. That division is based on the existence of the following gastric cancer groups:
I.   Diffuse
II. Intestinal (adenocancer)
III. Unspecified

Early gastric cancer

According to generally accepted definition of "Early gastric cancer" which was formulated by Japanese Gastroenterological Society in 1962 in cooperation with pathologists, it is the cancer in early stages of development, located on the mucous membrane, or mucous membrane and submucous membrane, but it does not penetrate into muscularis mucous membrane.

The Japanese classification, which was established on the basis of large clinical material, reduces macromorphological look of early gastric cancer into three main types with the following subgroups (1,5,6):
Type I – convex or polypoid type; lesions of this type have polypoid, nodular or villous appearance;

Type II – superficial, flat type; lesions of this type are divided into three subtypes: IIa-superficial type, raised above the surface of the mucous membrane. IIb-lesions at the same level as mucous membrane; IIc-flat lesions, a bit concave under the surface of the mucous membrane;

Type III – Excavated lesions in the form of smaller or larger ulcers.

Incidence of early gastric cancer

The more extensive criteria are used as indications for endoscopy, the larger the number of patients will be diagnosed with early gastric cancer, besides gastric cancer at advanced stage. According to Japanese authors, even up to 30% of surgically treated patients come in for examination at an early stage of gastric cancer (1-6), and therefore there is a very high rate of five-year survival. According to statistics of various groups, it varies from 90 to 95%. As for Europe, it is considered that in a well-organized endoscopic service there should be at least 10% of the total number of the diagnosed with early gastric cancer (1-6).

Aims

1. To establish the importance of gastroscopy as a reliable method for gastric cancer diagnosis.

2. To establish the importance of pathohistological result for localization and macroscopic result of gastric cancer, as well as the outcome and survival time in these patients.

Material and methods

The paper presents the investigation including 70 patients; they all had gastric cancer or adeno-cancer diagnosed with gastroscopy, and with pathohistological (PH) verification. Thirty-eight of them were treated with radical operation (total or subtotal gastrectomy) with systematic lymphadenoctomy; 15 of them were treated with palliative operation to improve their life quality, and 15 of them were treated with explorative laparotomy for establishing the final diagnosis and possible palliative operation, while 2 patients died because of bad health condition after endoscopic and pathohistological diagnosis had been made.

The data were retrospective-prospective, collected at the Health Care Centre Čačak in Čačak, for the period 2003-2006.

The data had diagnostic standard for gastric cancer which includes:
- anamnesis
- clinical examination
- lab analyses (blood count : HGB, HCT, MCV,Fe)
- stomach radiography
- gastroscopy with gastric biopsy and pathohistological verification (pH)
- digitorectal examination (cul de sac phenomenon)
- radiography of heart, lungs and bone system

The extended level of diagnosis in clinical conditions, in accordance with the clinical assessment, can be added by:
- stomach endosonography
- abdominal ultrasound, and scanner (CT) of abdomen with contrast if necessary
- tumor markers (CA-50, CA-19-9)
- laparoscopy
- explorative laparotomy

QUESTIONNAIRE FOR MALIGNANT DISEASES

-Full name _____
-Gender_____   -Age_____
-Address
-Gastroscopy
-Disease staging (Stage of a disease before operation-TNM classification used)

Stage of a disease after operation
- Histological tumor type
     - Diffuse
     - Intestinal
     - Unspecified
- Macroscopic look of a tumor:
     I. Fungal form
     II. Ulcerous form
     III. Ulcerous-infiltrative form
     IV. Diffuse-infiltrative form
-Lymphonodal status
-Operational type:
     1. Radical operation
     2. Palliative operation
     3. Explorative operation
Resection type:
     1. Total gastrectomy
     2. Subtotal gastrectomy
Outcome :
     1. Dead
     2. Alive

TNM classification

T1-Tumor invasion into mucous or submucous membrane, T2-Tumor invasion into m. propria or subserous layer, T3-Tumor penetration into serosa, T4-Tumor invasion into the surrounding structures.

N0- no evidence on lymphatic node metastasis, N1-metastasis in group 1 of lymphatic nodes, but no metastases in 2, 3,and 4 groups; N2-metastases in group 2 of lymphatic nodes, but no metasases in lymphatic nodes 3 and 4;

N3-metastasis in group 3 of lymphatic nodes, but no metastases in lymphatic nodes of group 4; N4-metastasis in lymphatic nodes of group 4.

P0- no peritoneal metastases; P1-metastases in the adjacent peritoneum, but no to the distant peritoneum; P2-a few metastases in distant peritoneum; P3-numerous metastases in the distant peritoneum. Adjacent peritoneum: peritoneum of smaller pouch and smaller and larger omentum.

H0-no liver metastases; H1-metastases within one lobe, H1 (dex)-metastases within the right lobe, H1 (sin)- metastases within the left lobe; H2-several metastases in both lobes; H3-numerous metastases in both lobes.

M0-no distant metastases except peritoneal or liver metastases.

M1-distant metastases except peritoneal or liver metastases

Category M1 should be specified according to the following markers:

Brain (BRA), Bone marrows (MAR), menings (MEN), Bone (OSS), Pleura (PLE), pulmonal (PUL), Skin (SKI) and other.

Statistical methodology

The given data were processed and presented in tables and graphs.

Description of the numerical marks in the paper was done by using classical methods of descriptive statistics with arithmetic mean and average of medium parameters, and among variable measures by standard deviation, coeficient of variation and standard error, as well as minimum and maximum values.

Relative numbers were used in all tables.

In the analysis of results, depending on the nature of the variables, Pirson's Chi square test was used in the form of the correspondance tests and contingency tables, for comparison of the difference between frequency of non-parameter features, for one or two features.

In numerical limitations of a table 2 times 2, Fisher's test of exact probability was used.

For comparison of the average values of parameters' features, the Student's t test was used for two groups of data. As non-parameter complements in independent samples, the rank sum test was used, and in dependable ones the test of equivalent pairs was used.

For comparison of three or more groups of data, Fisher's parameter variable analysis was used (ANOVA) for parametric data, and non-parameter variance analysis for non-parametric data proportions.

In connection analysis, the methods of simple and multiple correlation, and regression were used.

For the analysis of survival predictors and the occurence of hypertension, Cox's Proportional Hazardous method was used and logistics regression univariant for control with Log Rank Test for comparison among groups.

In all the applied analitical methods, the level of significance was 0.05.

For basis formation and data procession, the program of the Institute-Department for Medical Statistics and Informatics of Medical Faculty in Belgrade, was used.

Results

Frequency according to pH result

In Table 1, the frequency of our patients according to pH and tumor macroscopic result are presented.

Frequency analysis of our patients according to PH and tumor macroscopic result shows that there is statisytically very significant difference ($F=22.652$; $df=3$; $p<0.01$), and this is because in

intestinal tumors ulcerous-infiltrative and in diffuse diffuse-infiltrative results dominated.

Frequency analysis of our patients according to PH and final P tumor classification shows that there is a high statistically significant difference ($F=11.064$; $df=3$; $p<0.01$), and this is because in intestinal tumor, except P0 and P3 stages, all stages dominated, while in diffuse type, the P0 results were the most numerous.

Other parametres compared did no show any significant difference, according to the obtained PH tumor results.

Table 1. Frequency of our patients according to pH and macroscopic tumor result

		macroscopic look				Total
		Ulcerous infiltra-tive	diffuse infiltra-tive	ulcerous	fungal form	
PH	Intestinal	24	8	6	4	42
	Diffuse	5	20	1	0	26
Total		29	28	7	4	68

Table 2. Frequency of our patients according to final pH result and final P tumor classification

		Final P			Total
		P0	P1	P3	
pH tumor finding	intestinal	26	1	11	38
	diffuse	24	1	1	26
Total		50	2	12	64

Comparisons of numerical variables regarding outcome, pH result and cancer type

In Table 3, descriptive values of numerical variables regarding the outcome of the treatment of our patients are represented.

Table 3. Descriptive values of numerical variables regarding the treatment outcome

	outcome	N	median	SD
age	alive	26	63,07	11,25
	dead	44	66,29	10,79
Follow-up (days)	alive	26	335,61	61,00
	dead	44	96,95	92,36

Statistically significant difference was not found in average age values regarding the outcome of the cancer treatment, but it was reported for examination time (z was 11.937; $p<0.01$) and that period was on average four times longer in patients who survived.

Table 4. Descriptive values of numerical variables according to ph tumor result of our patients

	pH of tumor	N	Arithmetic mean	SD
age	intestinal	42	65,83	10,72
	diffuse	26	63,84	11,88
Duration of follow-up (days)	intestinal	42	138,59	126,50
	diffuse	26	230,38	111,94

In Table 4, descriptive values of numerical variables according to pH result in our patients are shown.

Statistically significant difference was not found in average values regarding age according to pH cancer result however, it was reported for the follow-up duration (z was 5.957; p<0.01), and that period was, on average, as twice as longer in diffuse tumors.
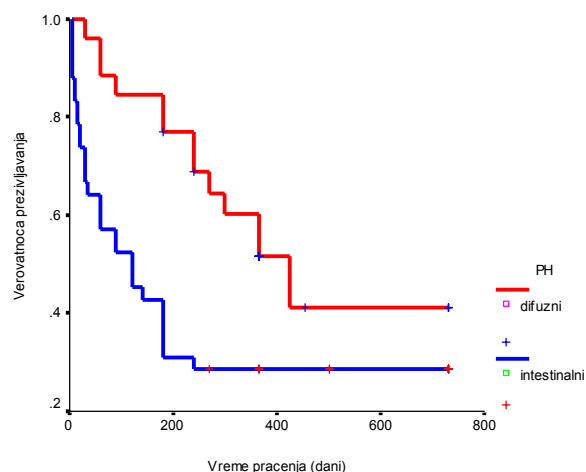
Survival analysis

In the analysis, statistically significant difference was found in survival time depending on cancer type (Log rank test is 3.785; p<0.05). Average survival time for adenocancers was about 90 days or 3 months, and for cancers 365 – about 12 months.
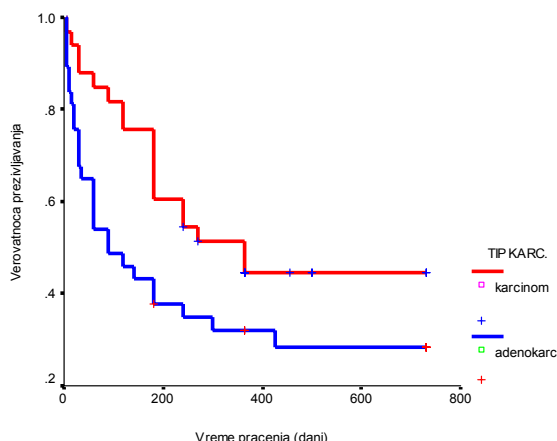
Graph 1 Probability of survival depending on cancer type

In the analysis, statistically significant difference was found in survival time according to PH cancer result (Log rank test is 6.392; p<0.01). Average survival time for intestinal cancers was about 120 days or four months, and for diffuse cancers about 425 days-14 months.

Graph 2. Probability of survival depending on cancer type

Discussion

Frequency according to pH result

The frequency analysis of our patients according to PH result and macroscopic tumor result shows that there is statistically highly significant difference, and this is because in intestinal tumors ulcerous-infiltrative one prevailed, while in cases of diffuse tumors, diffuse-infiltrative one dominated. Frequency analysis of our patients according to pH result and definite P tumor classification shows that there is statisti-cally highly significant difference, and this is because in intestinal tumor all stages, except P0 and P3, dominated, and in diffuse P0 results are the most numerous. The other parametres used did not show any significance according to pH tumor result in our patients. This is in accordance with literature data that imply that intestinal cancer type has slower development and better prognosis, while diffuse cancer type metastasizes through lymphatic system (1).

Comparisons of numerical variables regarding outcome, PH result and cancer type:

Statistically significant difference was not found in average age values regarding cancer treatment, but it was found in examination time and the period was on average four times longer in those who survived (5-6).

Statistically significant difference was not found in average age values according to pH cancer result, but it was found in the follow-up period, and that period was twice longer on average in cases of diffuse tumors. This is in keeping with literature data which indicate that early diffuse cancer has survival rate even up to 90% (1,5-8).

In the analysis, statistically significant difference was found in survival time depending on cancer type. Average survival time for adeno-cancers is about 90 days or three months, and for cancers 365 days-12 months. Literature data showed that intestinal cancer type-adeno-carcinoma has slower development and better prognosis (1, 5-8).

In the analysis, statistically highly significant difference in survival time was found according to pH cancer result. Average survival time for intestinal cancers is about 120 days or four months, and for diffuse cancers about 425 days or 14 months. Literature data showed that intestinal cancer type has five-year survival rate in 62%, while diffuse cancer type has five-year survival rate in 5% in comparison to the early type with survival rate of 90% (5-8, 9).

Conclusions

1. Gastroscophy is a reliable method for gastric cancer diagnosis.
2. Intestinal cancer type has slower development and better prognosis, and five-year survival rate in 62%
3. Diffuse cancer type metastasizes through lymphatic system, and is characterized by five-year survival rate in 5% in comparison to the early type in 92%.

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PATOHISTOLOŠKI NALAZ U DIJAGNOSTICI KARCINOMA ŽELUCA

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U ovom radu proučavno je 70 bolesnika sa karcinomom želuca koji su imali patohistološku verifikaciju. Cilj rada bio je da se utvrdi značaj gastroskopije kao suverene metode za dijagnostiku karcinoma želuca, kao i da se utvrdi značaj patohistološkog nalaza (PH) na lokalizaciju i makroskopski nalaz karcinoma kao ishod i dužina preživljavanja kod ovih bolesnika. Podaci su retsrospektivno-prospektivni. Zaključci su, pored potvrde suverenog značaja gastroskopije i da intestinalni tip karcinoma ima sporiji rast, bolju prognozu i petogodišnje preživljavanje od 62%; dok difuzni metastazira limfotokom i ima petogodišnju stopu preživljavanja od 5%, a rani 92%. Acta Medica Medianae 2009;48(3):15-19.

Ključne reči: gastroskopija, karcinom želuca, patohistološki nalaz