

# Comparability of Diagnostic Methods: Proximal Endoscopy, CT and EUS in Determining Stomach Tumor Localization and their Importance in the Preoperative Analysis of Process Progression

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## Original paper

### ABSTRACT

**Introduction:** Gastric cancer is one of the most common tumors in humans and is on the 14th place by frequency in the United States and it is at the 8th place by the mortality rate. In the world it takes seventh place by incidence. Today prevail the opinion and the surveys show, that it is twice as common in men as compared to women. Although there are advancements in diagnostics it must be noted that gastric cancer is still discovered late and when it already has metastasized, so that the therapeutic approach is limited and low survival rate. **Patients and Methods:** The study was retrospective-prospective, which covered the period from 2011 to 2012 and was performed at the Clinic of Gastroenterohepatology, Clinical Center of Sarajevo University. The study included 50 patients with gastric cancer, 34 men and 16 women. All patients underwent gastroscopy and according to tumor lesions localization divided into 3 regions: cardia, corpus and an-

trypyloric region. Tumor lesions were biopied with histologically confirmation of gastric wall cancer. All patients underwent CT of gastric wall, CT of the abdomen and in some cases EUS was performed also. Goal: To prove by available diagnostic methods (endoscopy, CT and EUS) the presence of gastric cancer, histologically validate it and determine localization according to regions. To determine by CT the thickness of the stomach wall or the penetration of tumor lesions, the presence of enlarged lymph nodes and possible metastases. Record by EUS the progression of malignant processes in depth to layers of the wall, surrounding tissue metastases and enlarged lymph nodes. Determine the correlation between the measured parameters. **Results:** Our study showed that the localization of tumors at the cardia was represented in 15.31%, corpus in 17.36% and antropyloric region 16.33%. Median age he was 65.5 years with a standard deviation of 11.04. We failed to demonstrate a statistically significant difference in verified findings by EUS and age as

well as endoscopic findings and age. Also there is no statistically significant difference between the CT scan and endoscopy  $XT = 5.99$  and  $\alpha = 0.05 = 0.63 XE, XE < Xt$ . There is a significant difference between the results of CT by age groups ( $XT = 3.84$  at  $\alpha = 0.05, XF = 0.05, EE > XT$ ) and endoscopic findings and age ( $XT = 3.84$  at  $\alpha = 0.01, = 0.01 XE, XE > XT$ ). **Conclusion:** Our study showed that gastric cancer are more common in men than women, metastases were more common in the elderly population, there were no significant deviations from the endoscopic findings and CT findings. EUS was performed in a small number of patients and showed as a good method because it gave accurate information about the penetration depth. Endoscopy, EUS and CT are ideal methods in diagnostic and staging of gastric cancer before the surgery.

**Key words:** CT (computed tomography); EUS (endoscopic ultrasound); gastric cancer; endoscopy.

## 1. INTRODUCTION

The incidence of gastric cancer significantly varies, depending on the country and population, with higher rates among the lower class social groups which during 1930 in the U.S. had a high mortality rate, but its incidence decreased over the past 60 years. Gastric cancer is two times more common in men than women and is more common in Af-

rican Americans compared to the Caucasians in the United States (1). While showing decline in incidence, still is present drastic increase in cardia cancer, which is now considered a separate entity in gastroenterology. Gastric cancer ranks as 14<sup>th</sup> among those suffering from cancer in the United States and the eighth by the rate of mortality with 14700 deaths each year. High risk

of developing gastric cancer showed the countries of Central and South America, as well as most of the Far East countries with a lower incidence in the United States and Canada, the Middle East and different variations in Commonwealth countries with a high level of risk in the countries of Europe. Gastric cancer is one of the highly lethal diseases with a 5 years survival rate of less than 20%. This

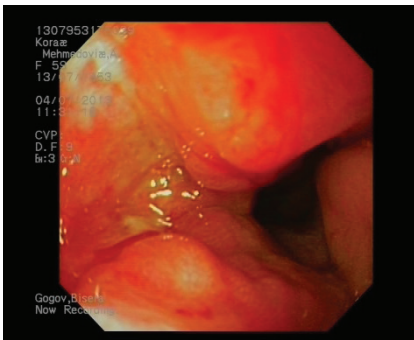


Figure 1. Endoscopic image of gastric cancer

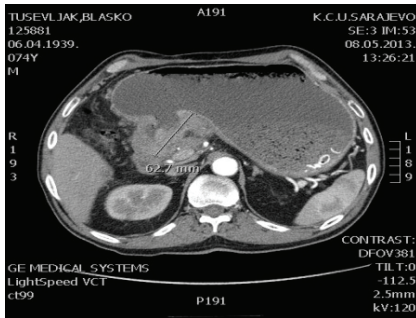


Figure 2. CT image of a stomach tumor process



Figure 3. Presentation of gastric cancer by EUS

tologically analyzed. (figure 1,2,3).

In order to assess the involvement of the wall and the penetration depth of infiltration, patients underwent CT of the gastric wall.

Some patients also underwent EUS (endoscopic ultrasonography) which tracks penetration of infiltrate in the layers of the stomach wall. Metastatic changes are recorded both by the CT and the EUS.

## 2. MATERIAL AND METHODS

The study was of prospective retrospective character, performed at the Clinic of Gastroenterohepatology, Clinical Center of Sarajevo University. The study included 50 hospitalized patients, 16 women and 34 men for a period of two years (2011-2012). Upon admission all patients underwent targeted gastroscopy with mucosal biopsy samples taken and sent for histopathological diagnosis at the Institute of Pathology, Medical Faculty in Sarajevo. By endoscopy as a visual method, we evaluated the changes in the mucosa, and accurately localize them by region. Stomach have been divided into three regions; cardia, corpus and antropyloric region. Gastroscopy as the gold standard in detection of changes in the mucosa, which allows the exact localization of changes, targeted biopsy and monitoring therapeutic effect of change in control endoscopy. Experienced endoscopists during procedure follows the peristalsis of observed organs as well as the targeted region. Macroscopically it can track changes in size, penetration into the surrounding mucosal edema and changes in the tumor region. Endoscopically or macroscopically are visually evaluated different regions of the stomach, so that each region in the gastric mucosa has its

visual characteristics. Patients have been divided into two groups. The first were women, 16 of them and the other men, 34 with recorded age in all cases.

Patients underwent CT of gastric wall and abdomen and some of them EUS. Biopsy samples are sent to the Institute of Pathology in bottles with formalin, where they were deposited after the biopsy. They were treated in order that was cut and stained with eosin and sometimes were analyzed by immunohistochemical analyzes. Then the pathologist gives histopathologic analysis and confirmed clinical diagnosis. Obtained clinical findings during diagnostic staging were analyzed statistically.

## 3. GOALS

\* By available diagnostic methods (endoscopy, CT and EUS) prove the presence of gastric tumor, histologically verify diagnosis and localize the regions.

\* By CT determine the thickness of the wall of the stomach or the progression of tumor lesions, the presence of enlarged lymph nodes and eventual metastasis.

\* Record by EUS progression of malignant processes in depth to layers of the wall, surrounding tissues metastases and enlarged lymph nodes.

\* Determine the correlation between the measured parameters.

## 4. RESULTS

The initial data table containing data about patients' age, gender and remarks about CT, EUS and Endoscopy was used for performing this analysis. The endoscopy was performed in all patients, and for some CT and EUS procedure weren't performed. At first, all patients were grouped into five age groups. The number of groups was reduced to three, because there wasn't enough data for the analysis of contingency tables of interest. Majority of patients belonged to the age group 56-75 years (29 or 60.4%), then to the age group 76 year and older (10 or 20.8%) and the least number to the youngest age group younger than 55 years (9 or 18.8%). See figure 4,5,6,7.

Among the group of patients, the

is a disease of middle age and is most common in age of 55 while it is rare in younger persons up to age of 30 years (2). According to the anatomical distribution in the U.S. there is a noticeable increase in the incidence of cancer at cardia, distal third of the esophagus and gastroesophageal transition. It is widespread among Caucasian population. Occurrence of gastric cancer is influenced by numerous risk factors. One that deserves special attention is the dietetic hypothesis. It emphasizes the importance of N-nitroso components of dietary sources involved in the development of gastric cancer. Smoking and alcohol consumption have a strong impact. H. pylori is maximally involved in the formation of precancerous lesions of the stomach lining, leading to the development of gastric adenocarcinoma. Among the poor population in countries with lower economic status, gastric cancer is often localized at the antrum along the smaller curvature and antero-corpus crossing. It is more common in enteropyloric region compared to cardia (3).

Proximal endoscopy as the gold standard is used to diagnose changes in the gastric mucosa. Macroscopic changes are noted and underwent targeted biopsies which are then his-

number of males (32 or 67%) was higher than the number of females (16 or 33%). The average age of all patients is 65.5, with standard deviation of 11.04.

Depending on the cancer localization under the endoscopy distribution was fairly similar with 17 or 36% of cancers located at the antropyloric region, 16 or 33% at the cardia and 15 or 31% located at the corpus.

The precision of endoscopy was tested by the CT. For that purpose, CT procedure was done in 37 patients. It turned out that CT confirmed diagnosis in majority of cases (59.5%).

Further analysis was performed in order to describe data collected in this research. For this purpose, the chi-square test was chosen. The chi-square test is used to determine whether there is a significant difference between the expected frequencies and the observed frequencies in one or more categories [4]. Due to small number of cases, the age was regrouped into two groups: 56-75 as the most numerous group, and others.

The results of testing imply that there is no statistically significant difference in EUS by age ( $\chi_T=3.84$  at  $\alpha=0.05$ ,  $\chi_E=0.48$ ;  $\chi_E < \chi_T$ ), as well as for the difference in and age/endoscopy tests ( $\chi_T=3.84$  at  $\alpha=0.05$ ,  $\chi_E=0.05$ ;  $\chi_E < \chi_T$ ). Regarding gender, the results showed again no statistically significant difference in CT by gender ( $\chi_T=3.84$  at  $\alpha=0.05$ ,  $\chi_E=0.36$ ;  $\chi_E < \chi_T$ ). Finally, we tested if the results of CT confirm the results of endoscopy. The results suggest the absence of statistically significant difference between these ( $\chi_T=5.99$  at  $\alpha=0.05$ ,  $\chi_E=0.63$ ;  $\chi_E < \chi_T$ ).

On the other hand, there is statistically significant difference CT

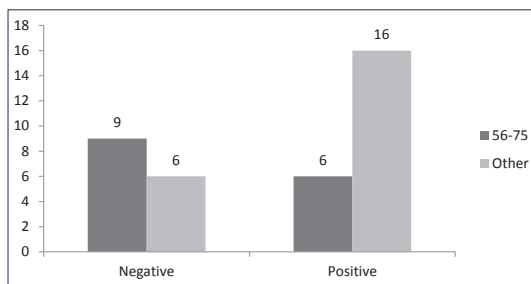


Figure 4. Histogram of the contingency table showing the comparison of cancer localization through endoscopy and CT (Negative means that CT did not confirm endoscopy).

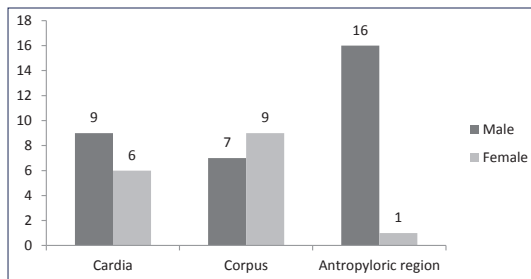


Figure 5. Distribution of localization of cancer after endoscopy.

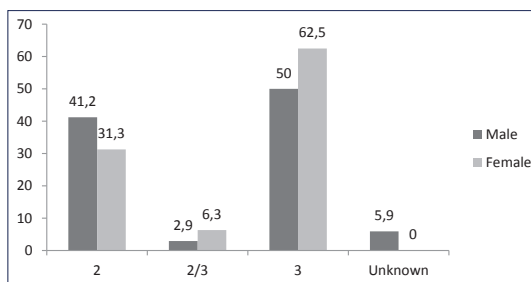


Figure 6. Comparison of tumor grade by gender

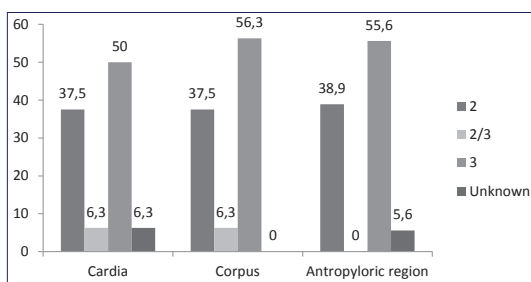


Figure 7. Comparison of tumor grade according to tumor location

results by age groups ( $\chi_T=3.84$  at  $\alpha=0.05$ ,  $\chi_E=0.05$ ;  $\chi_E > \chi_T$ ) and endoscopy by gender ( $\chi_T=3.84$  at  $\alpha=0.01$ ,  $\chi_E=0.01$ ;  $\chi_E > \chi_T$ ).

Furthermore, it turns out that the results of endoscopy are related to gender, implying that feminine patients are more likely to have localization in Reg1, or Reg2, unlike male patients, as presented in Figure 5.

Analysis of tumor grade shows that more than half of the patients had tumor grade 3 (27 or 54.0%) followed by grade 2 (19 or 38%), and the

least number of patients grade 2/3 (2 or 4.0%) with 2 cases in which the grade was unknown at the time of study.

The analysis was performed by chi-square with Yates correction, given that the cells are present in the table with the number of cases less than five.

Statistical analysis indicates that although there are variations between the sexes in terms of greater representation of tumor grade 2 (41.2%) in men, and a large number of patients with grade 3 (62.5%), a significant difference was not detected ( $p > 0.05$ ).

There are slight differences in terms of greater representation of grade 3 in women but because of the small number of individual cells chi-square test with Yates's correction did not reflect statistically significant differences.

## 5. DISCUSSION

So far, conducted studies have shown that the presence of well-differentiated cancer cells and microvascular invasion play a major role in the progression of gastric cancer and metastatic lesions.

Noninvasive imaging techniques such as CT, MRI and U.S. have great significance in assessing resectability and prognosis of cancer (5).

Analyzing demographic data, our results showed that from the 50 patients included in the study were 34 men and 16 women at mean age of 65.5 years. Compared to other researchers there was no major deviations (5).

Results of the study by Yin XD et al. shown that in the rural areas among the elderly population over the last 20 years there is the growth of metastatic gastric cancer, as a result of intratumoral microvessel and lymphatic invasion of cancer cells (5). Intratumoral microvessel and lymphatic invasion of cancer cells is closely correlated with lymph node metastasis of gastric carcinoma and poor prognosis of survival. CT scan is highly significant in the preoperative assessment of surgical resectability of gastric cancer.

Analyzing the results of our research, or presence of metastases

in the total sample, we have found that more than half of the patients were free of metastasis. In patients who had distant metastases, we came to conclusion that the most frequent localization was the liver in a group of 18 patients (36%), and of that number, one patient had beside metastatic liver changes in the peritoneum and 1 in the lungs. In remaining cases metastases were reported in the peritoneum, spleen and one in the pancreas.

Significant difference is found between the genders. Due to the small number of patients could not be calculated statistically significant difference between localization of tumors and metastases. Analyzing age group metastases were more common in older age groups, which is consistent with the results of the study by Yin XD et al. (5)

In histological analysis of gastric carcinoma bioptic samples, our research has shown that more than half of the patients had grade 3 (27 or 54%). Grade 2 was found in 19 or 38% and grade 2/3 at 2 or 4% of patients. In 2 cases the grade was unknown. Statistical analysis showed that although there is variation between the sexes in terms of greater representation of grade 2 in men (41.2%), and more with grade 3 (62.5%), the difference was not significant ( $p > 0.05$ ). We notice that in women representation of grade 3 was slightly higher but due to small sample we could not prove statistical significance. Compared to other researchers such as one by Staniuk T. and associates (7) which found grade 2 in 12 patients and grade 3 in 13 patients and 25 patients did not specify the grade, we find that more than half of the patients in our group of patients had grade 3.

Our research has shown a good correlation between the endoscopic findings and CT of the gastric wall in the assessment of process progression and its localization which is in agreement with the research by Kaya AO et al. that found a high rate of detection of a tumor process in cancer patients (6).

Then was analyzed the accuracy of endoscopic ultrasound findings in relation to the age of the patient when

they found that there was no statistically significant difference between the findings of EUS and age groups. Since we had a small number of patients who underwent EUS could not calculate the statistical significance, but we can determine that EUS is very accurate in proving the involvement of stomach wall and its layers, closer metastases in neighboring organs and lymph nodes but is unreliable in detecting distant metastases (8).

EUS is a diagnostic method that is likely to occupy the first place in the diagnostic staging of gastric cancer, as it gives information about the exact depth of involvement of the gastric wall, so that the abdominal surgeon has informations before surgery about localization and depth of invasion of malignant lesions as well as the involvement of the surrounding lymph nodes and any metastases in neighboring organs. Similar opinion had Tomizawa M et al. (9).

We wanted to compare EUS with CT scan, but due to the small number of the performed EUS could not get significant values. Our EUS findings were confirmed by endoscopic localization as well as metastasis to the neighboring organs and depth of wall involvement in the malignant process.

Baiwen Li et al. have a larger sample are compared CT and EUS, and came to the conclusion that EUS and CT represents ideal combination in the diagnosis and preoperative staging of patients with gastric cancer (10).

It was also found that there is a statistically significant difference between the endoscopic findings and the patient's age ( $XT = 3.84$  at  $\alpha = 0.01$ ,  $= 0.01$  XE,  $XE > XT$ ) and CT patients and age where ( $XT = 3, 84$  at  $\alpha = 0.01$ ,  $= 0.01$  XE,  $XE > XT$ ).

Finally, we analyzed whether the results of the CT findings were compatible endoscopy. The results evaluation showed a lack of significant differences between the studied parameters.

## 6. CONCLUSION

Conclusion: Endoscopy, CT and EUS are currently the most accurate

diagnostic protocols in detecting tumors, validating penetration and involvement of the gastric wall by malignancy as well as in detecting enlarged lymph nodes and metastases. Future studies on a larger number of patients should confirm the position of these diagnostic methods in the diagnosis of disease and preoperative staging.

## REFERENCES

1. Correa P. Human Gastric Carcinogenesis: A Multistep and Multifactorial Process. First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. *Cancer Research*. 1992; 52: 6735-6740.
2. Correa P. Helicobacter pylori and Gastric cancer. *State of the Art. Cancer Epidemiology*. 1996; 5: 477-481.
3. Vukobrat-Bijedic Z. Karzinom zeluca: prekancerozne lezije i prekancerozna stanja. 2008; 11-91.
4. Sharp V. *Statistics for the Social Sciences*, Little Brown & Co, 1979.
5. Yin XD, Huang WB, Lu CY, Zhang L, Wang LW, Xie GH. A preliminary study on correlations of triple-phase multislice CT scan with histological differentiation and intratumoral microvascular/lymphatic invasion in gastric cancer. *Chin Med J*. 2011; 124(3): 347-351.
6. Kaya AO, Coskun U, Unlu M, Akdemir Uo, Ozdemir NY, Zengin N, Benekli M, Yildiz R, Yamain E, Ozturk B, Gumus M, Uner A, Yamac D, Ucgul E, Buyukberber S. Whole body 18F-FDG PET/CT imaging in the detection of primary tumors in patients with a metastatic carcinoma of unknown origin. *Asian Pac J Cancer Prev*. 2008; 9(4): 683-686.
7. Staniuk T, Zegarski W, Malkowski B, Jankowski M, Klag M, Pietrzak T. Evaluation of PLT-PET/CT usefulness in diagnosis and qualification for surgical treatment of gastric cancer. *Wspolczesna Onkol*. 2013; 17(2): 165-170.
8. Hallinana JT, Venkates SK. Gastric carcinoma: imaging diagnosis, staging and assessment of treatment response. *Cancer Imaging*. 2013; 30: 212-227.
9. Tomizawa M, Shinozaki F, Hasegawa R, Fugo K, Shirai Y, Ichiki N, Sugiyama T, Yamamoto S, Sueioshi M, Yoshida T. Screening Ultrasonography is Useful for the Diagnosis of Gastric and Colorectal cancer. *Hepatogastroenterology*. 2013; 60(123).
10. Baiwen Li, Ping Zheng, Qi Zhu and Jun Lin. Accurate Preoperative Staging of Gastric Cancer with Combined Endoscopic Ultrasonography and PET-CT. *Tohoku J Exp Med*. 2012, 228: 9-16.