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# A Correlative Study of Histology and Imprint Cytology of Gastric Mucosa Byopsy in the Diagnosis Gastric Cancer

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**A B S T R A C T**

*The purpose of this paper is to show the importance of gastric mucosa imprint cytology in detecting stomach cancer. Analyzed were 364 cytological and pathohistiological samples taken from 335 patients having suspected diagnosis of gastric cancer. Every specimen was submitted to slide imprinting and then fixed in formalin for further processing with routine histopathology. The imprints were air dried for cytological analysis, stained according to May-Grünwald-Giemsa and analyzed by light microscope.*

*By pathohistological punch-biopsy samples analysis stomach cancer was found in 45 samples. With cytologycal samples analysis the cancer was detected in 48 samples and 13 cytological samples were suspected of cancer. With combining these two methods cancer was found in 68 cases. Patients with positive cytological finding and negative pathohistologic finding underwent gastroscopy with punch-biopsy. All patients with positive patohistological findings were operated. All materials were histologically examined. Cancer was found in 68 patients. Cytological analysis of stomach mucosa bioptic material imprints, increases the number of positive findings in preoperative stage of gastric cancer diagnosis. The greatest advantage of this method is short period for preparation of material, simplicity and low price. Every data on morphological changes in mucosa has been also pathohistologically checked, because taking imprints does not damage the specimen.*

***Key words:*** *imprint cytology, gastric mucosa biopsy, gastric cancer*

## Introduction

As in most malignant diseases gastric cancer prognosis and survival with other factors mostly depend on percentage of spreading when the disease was diagnosed, therefore early detection of disease is of greatest importance. Japanese authors were first to observe and describe the early cancer (T1N0M0), depending on depth of stomach infiltration, metastasis in lymph nodes or distant organs[1]. It was proved that such patients have significantly better prognosis and that 95% of them lived another 5 years[2]. In eighties 2.8–4.2% of patients in TIN0M0 stage of disease in Europe and USA were treated while in Japan 66% of operated patients were in T1N0M0 stage of disease. The reason for these good results was implementation of esophagogastroduodenoscopy with possibility of taking specimens for cytology and histology with screening of endangered population[3,4].

As far as other body sites, are concerned the examination of exfliative cytologic specimens that were taken from gastrointestinal tract was not used for number of years. Mostly, it was because of lack of satisfactory processes for collecting sufficient number of well-preserved cells from these digestive organs[5]. In 1947 Papanicolau and Cooper reported a gastric lavage method for collecting cells from the stomach. Later, Papanicolau and colleagues introduced a blind abrasive gastric balloon[5]. However, the present diagnostic era arrived with development and more widespread usage of flexible fiberoptic

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**TABLE 1**
STATISTICAL ANALYSIS OF THE DATE

| | Cytology | Punch byopsy | Combined | Operative Hystology |
|---|---|---|---|---|
| True positives | 61 | 45 | 68 | 68 |
| True negatives | 289 | 289 | 289 | 0 |
| False positives | 2 | 0 | 2 | 0 |
| False negatives | 12 | 30.00 | 5 | 0 |
| Sensitivity (%) | 83.56 | 60.00 | 93.15 | 0 |
| Specificity (%) | 99.31 | 100.00 | 99.33 | |
| False positive rate (%) | 0.69 | 0 | 0.67 | |
| False negative rate (%) | 16.44 | 40.00 | 6.84 | |
| PV of a positive result (%) | 96.83 | 100.00 | 93.15 | |
| PV of a negative result (%) | 96.01 | 91.40 | 98.34 | |
| Prevalence rate (%) | 20.05 | 19.03 | 19.68 | |

endoscopes for upper gastrointestinal tract, coupled with visually directed samplings of lesions[2,6,7,8].

This study reviewes the reliability and efficiency of the cytodiagnosis of imprint cytology of gastric mucosa biopsy obtained under direct vision, during esophagogastroduodenoscopy in 335 patients. The purpose was to evaluate role of cytology in establishing the diagnosis of gastric cancer.

## Materials and Methods

During five-year period, to be exact from January 1, 1997 to December 31, 2001, 364 punch biopsy samples were taken from 335 patients that had clinical or endoscopic suspicion on gastric cancer. 75 patients were operated because they had cytological and/or histological gastric cancer diagnosis. All materials were completely histologically examined. Gastric cancer was found in 68 operated patients. Four operated patients had gastric polyps, two had peptic ulcers, and one was operated because was suspected of early gastric cancer although no cytological or pathological finding cancer. In 289 patients gastric carcinoma was not detected. Although they were monitored for number of years. In patients with preoperative positive cytological and negative pathohistological findings endoscopic examination was repeated and in 335 patients specimens for cytological and pathohistological analysis were taken 364 times. For final comparison of methods, excluded were the cancer patients who at the time of diagnosis were inoperable, patients that did not have cytological samples, patients that have been operated as urgent cases without prior preoperative morphologic diagnosis and patients operated in other institutions, for whom pathohistological finding could not be obtained.

In gastric biopsy, 1–3 samples to were analyzed per patient. Each specimen was firstly submitted to slide imprinting and then formalin fixed for routine histopathology. Imprints were air dried, stained by May Grünwald-Giemsa method (MGG) and analyzed by a light microscope. Then the specimens were fixed in 10% buffered formalin, paraffin embedded, cut into 5 μm sections, stained with hemalaun-eosin (HE) and analyzed by a light microscope[9,10].

Based on cytological diagnostic criteria for gastric cancer, the cytological specimens were classified in 3 categories: positive, suspicious and negative. For this study, the findings of cytology and histology on the biopsy sample, the postoperative diagnosis (including histopathology) and the follow-up were compared for each of the 335 cases with definitive diagnosis. Based on final diagnosis, the cytological and histological diagnosis of the biopsy sample in each case were categorized as true positive (TP, including positive and suspicious diagnoses), true negative (TN, including negative and unsatisfactory findings), false negative (FN) and false positive (FP)[11].

Collected data were statistically evaluated with method of Galen and Gambino. The following standard formulae were used: sensitivity = TP/(TP+FN)x100; specificity = TN/(TN+FP)x100; false positive rate (FP) = FP/(FP+TN)x100; false negative rate (FN) = FN/(FN+TP)x100; PV of a positive result = TP/(TP+FP)x100; PV of a negative result = TN/(TN+FN)x100; prevalence rate = (TP+FN)/(TP+TN+FP+FN)x100[11]. The overall diagnostic accuracy is the probability of the patients being correctly identified as true positive and true negative by the cytological test.

## Results

In the period of five years, 364 fiber-endoscopic biopsies were done in 335 patients because of suspicion on stomach cancer. Malignant cells were found in 61 cytological samples. Cancer diagnosis was made in 45 histological samples. 75 patients were operated because of cytological and/or pathohistological (punch biopsy) cancer diagnosis. All materials were completely histologically examined. Stomach cancer was found in 68 operated patients. Excluded were patients with malignant diseases who at the time of diagnosis were inoperable, patients from whom cytological sample was not taken, patients that were urgently operated without preopera-

tive morphologic diagnosis and patients operated in other institutions, for which pathohistological findings could not be obtained.

The cytological findings in 364 cytological samples were positive in 48 (13.2%) cases, suspicious in 13 cases (3.57%) and negative in 289 (79.4%). Compared to final diagnosis (operative histology), there were 61 TP (89.7%), 289 TN, 12 FN and 2 FP cytological diagnoses. This gave sensitivity of 83.56%, specificity of 99.31% FN rate of 16.44%, FP rate of 0.69%, and PV of a positive result of 96.83%, PV of a negative result of 96.01% and prevalence rate of 20.05%. If we combine endoscopic cytology and histology, sensitivity increases to 93.15%, and decreases the false negative rate to 6.84% (Table 1).

Twelve FN cases included 12 cases of adenocarcinoma (8 reported as chronic gastritis, 1 as gastric polyp and 3 as peptic ulcers). 2 false positive cases included 1 peptic ulcer and 1 gastric polyp. While FN results were due to various factors, including method of taking material, number of taken samples, place where samples were taken and misinterpretation. All of FP results were due to misinterpretation.

## Discussion and Conclusion

Number of described tumours in this paper does not represent absolute number of checked and operated patients in our hospital. We considered the patients who had esophagogastroduodenoscopy, punch-biopsy, cytological samples and hystologycal samples and well-known final diagnosis (operative histology or clinical monitoring). Some of the patients were operated and further treated in other institutions, some were inoperable at the time of setting diagnosis, and some of them were operated urgently, without making prior endoscopic and/or cytologycal and pathohistological diagnosis. For patients with positive cytological findings and negative pathohistological findings examination was repeated immediately or in intervals of one to three months, and after that they were monitored for at least one year.

Nowadays, brush specimens is mostly frequently used method of taking material for cytology[12,13]. The same method was also used in our institution when the examination was introduced. Material was directly placed from the brush to the slides. As we were not satisfied with quantity and quality of material and results we switched to imprint method. Kathleen[14] describes that washing endoscope canal gives 91% positive results. Crisoula[15] says that imprint method gives 94.4% positive findings. Our result of 89.71% positive samples on five year material obtained by imprint method coincide literature (78–94.4%)[16–20].

Sensitivity of 83.56% satisfies, particularly because the number of false positive diagnoses was kept to a minimum (specificity 99.31%). This sensitivity is similar to the ones reported by other centres. The cytological examination gave false positive results in 2 samples (0.69%), for which biopsies were negative. Sensitivity in tracked period for punch biopsy histology was 60%, and with combining two methods increased to 93.15%. The number of false negative cytologycal samples is 12 (3.3%) and false negative histological samples 30 (8.24%). Combining two methods number of false negative samples was reduced to 5 (1.37%). For false negative samples beside other factors important is the number of taken samples. Increasing the number of samples, taken from multiple locations increases the number of positive cytological and pathohistological findings (with some authors even above 90%), what opens the question of simultaneous taking cytological samples.

Great numbers of authors recommend using both methods because it increases the percentage of preoperatively exactly made diagnoses. Cusso states that both methods should be used, because using cytology only in selected cases can give poor results and therefore discourage doctors to use it[16]. In our case, where neither method had sensitivity over 90%, and when using the two methods sensitivity raised to 93.15%, significance of using two methods is not questionable. Besides, gastric mucosa imprint cytology is fast, simple and cheap method for detecting stomach cancer, and characterized with high sensitivity and specificity as compared with histopathology.

We might conclude that usage of esophagogastroduodenoscopy with cytology and histology increases the number of preoperatively made diagnoses, but does not increase the number of patients that were detected in T1N0M0 stage of diseases. The increase in number of diagnosed patients can be achieved only by screening of endangered population.

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## USPOREDNA ANALIZA HISTOLOŠKIH NALAZA I CITOLOŠKIH NALAZA OTISKA BIOPSIJE ŽELUCA U DIJAGNOZI KARCINOMA ŽELUCA

### S A Ž E T A K

Cilj ovoga rada bio je ustanoviti vrijednost citološke analize otiska ekscidirane sluznice želuca u otkrivanju karcinoma želuca. Analizirano je 364 bioptata kod 355 bolesnika kod kojih je endoskopskim pregledom postavljena sumnja na karcinom želuca. Od svakog uzorka najprije je načinjen preparat otiska na staklo, a zatim je uzorak fiksiran u formalinu za daljnju rutinsku patohistološku obradu. Preparat je za citološku analizu osušen na zraku, bojan metodom po May-Grünvald-Giemsi i analiziran svjetlosnim mikroskopom. Patohistološkom analizom karcinom želuca nađen je u 46 uzoraka, a citološki u 48 uzoraka, dok je 13 citoloških uzoraka bilo suspektno na karcinom želuca. Kombinirajući ove dvije metode nađen je karcinom u 68 uzoraka. Bolesnicima koji su imali pozitivan citološki nalaz, a negativan patohistološki nalaz ponovljena je ezofagogastroduodenoskopijaskopija sa biopsijom. Svi bolesnici sa pozitivnim nalazom su operirani i dobiveni materijal je u cijelosti patohistološki pregledan. Karcinom je nađen kod 68 bolesnika. Citološka analiza preparata otiska bioptičkog materijala sluznice želuca povećava postotak pozitivnih nalaza u preoperativnoj dijagnozi karcinoma želuca. Najveća prednost metode je brzina, jednostavnost i niska cijena. Svaki podatak o morfološkim promjenama sluznice provjerava se i patohistološki jer uzimanje otiska ne oštećuje uzorak.