

# Study of Histopathological Parameters of Gastric Carcinomas with Micropapillary Component

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**ABSTRACT:** Micropapillary carcinoma was recently identified as a carcinoma variant characterized by the presence of small clusters of tumor cells located in optically empty spaces. The study included a number of 14 cases represented by surgical excision specimens diagnosed with gastric carcinoma (tubular, papillary and signet-ring) which associated the micropapillary component in variable proportions. Regarding the low-grade tubular carcinomas, the micropapillary component represented less than 25% of the tumor, while in the high-grade tubular carcinomas and papillary carcinomas it represented 25-50%. Among signet-ring carcinomas, the micropapillary component had a percentage of over 50. The depth of invasion was frequently associated with T3 and T4 categories. Lymph nodes metastasis were found in ten cases and distant metastasis were present in three cases. Recognition of the micropapillary component associated with gastric carcinoma represents an aspect of great importance because it is frequently correlated with unfavorable prognosis parameters.

**KEYWORDS:** Gastric carcinoma, micropapillary component, histopathological parameters.

## Introduction

Gastric carcinoma represents the second most common cause of cancer related mortality worldwide. Several classifications of gastric cancer have been proposed over time, but Lauren and WHO classifications are most commonly used in clinical practice [1].

In recent years, early detection, endoscopic mucosal resection for early gastric cancer and neoadjuvant therapy have led to remarkable advances in the management and prognosis of this neoplasia. Thus, prediction of the aggressive behavior and precise risk stratification for some variants of gastric cancer has become of crucial importance.

Micropapillary carcinoma has recently been identified as a type of carcinoma, characterized by the presence of small clusters of tumor cells located in optically empty spaces [2-5].

This entity has been reported in various locations, more commonly in the mammary gland, urinary bladder, lung, major salivary glands [2,4-6], and the gastrointestinal tract [7-9]. Although reports on gastric cancers with micropapillary component are limited, several studies have shown a high frequency of lymphovascular invasion and lymph nodes metastasis [7,10,11].

We aimed to analyze some histopathological aggressiveness parameters of various subtypes

of gastric carcinomas related to the percentage of the micropapillary component.

## Material and Methods

The present study included a number of 14 cases of gastric carcinomas which incorporated the micropapillary component in various proportions. The biological material was represented by surgical excision specimens obtained from the Surgical Clinics of the Emergency County Hospital of Craiova. The histopathological diagnosis was performed in the Laboratory of Pathology of the same hospital where the specimens were fixed in 10% neutral buffered formalin, automated processed by paraffin embedding and hematoxylin-eosin stained. Data interpretation was performed with the Nikon microscope Eclipse E600 and software program Lucia 5.

The tumors classification has been achieved according to the latest WHO recommendations [1].

For the selected cases, we followed a series of histopathological parameters such as tumor type, depth of invasion, lymphovascular invasion, presence/absence of lymph node metastasis and distant metastasis, in relation with the micropapillary component percentage. The micropapillary component was estimated to be between  $\leq 10\%$ , 10-25%, 25-50%, and  $\geq 50\%$ , by two independent specialists (CS and AS).

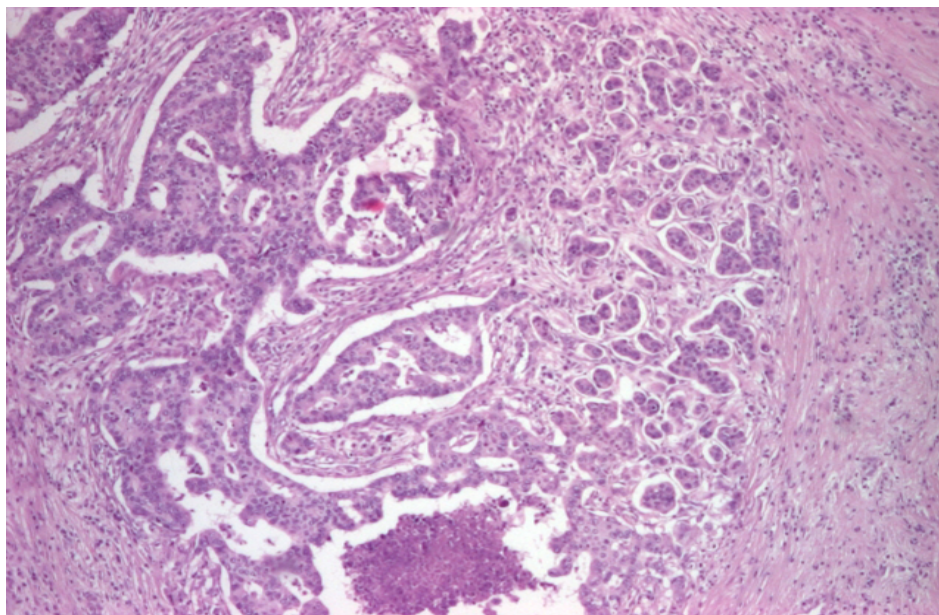
The study was approved by the local ethical committee (no 201/24.10.2017), and written informed consent was obtained from all the patients.

## **Results**

The 14 analyzed gastric carcinomas cases were diagnosed in patients with a mean age of

64.3 years, predominantly males (male/female ratio: 2.5/1).

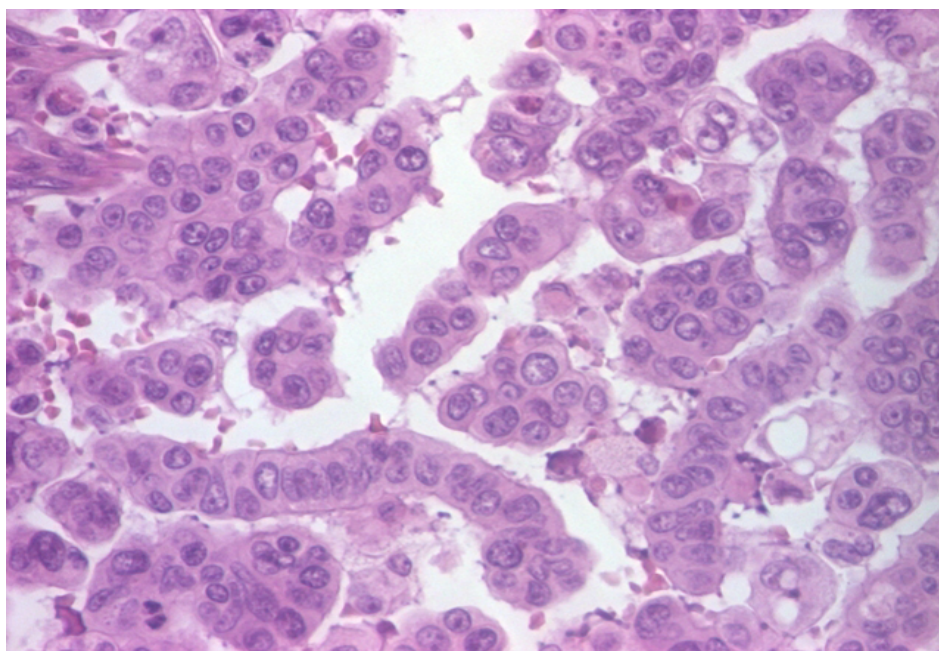
Tumors were tubular, papillary or signet-ring gastric carcinomas associated in variable proportions with a micropapillary component (Table 1) (Fig.1).



**Fig.1. High-grade tubular gastric carcinoma with micropapillary component, HE staining, x100**

The micropapillary component consisted of carcinomatous cells with moderate to severe atypia and a moderate amount of cytoplasm, realizing aspects of micropapillary structures without obvious connective-vascular axis.

Micropapillary structures were observed in some cases only in the deep part of the tumors, surrounded by an empty optical space, with the appearance of a retraction artifact (Fig.2).



**Fig.2. Gastric carcinoma, micropapillary component without obvious connective-vascular axis, HE staining, x100**

The lacunar spaces around the micropapillary aggregates were limited by delicate fibers of fibrocollagenous stroma which had a similar appearance with blood vessels or lymphatic vessels.

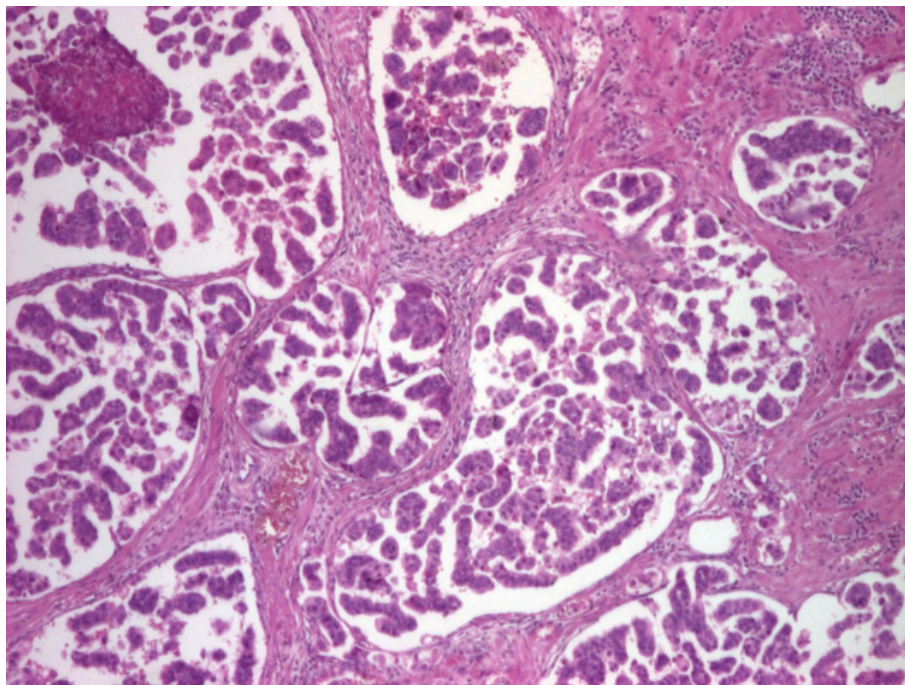
The micropapillary component represented less than 25% in low-grade tubular carcinomas; the high-grade tubular carcinomas and the papillary carcinomas associated the micropapillary component in 25-50% of the tumor, while among the three cases of signet-ring carcinomas, it represented 75-90%.

**Table 1. Correlation between histopathological parameters and the micropapillary component percentage**

Histopathological parameters		<10%	10-25%	25-50%	>50%
Type of carcinoma	Low-grade tubular carcinoma	5	2	0	0
	High-grade tubular carcinoma	0	1	1	0
	Low-grade papillary carcinoma	0	0	2	0
	Signet-ring carcinoma	0	0	0	3
Lymph vessel invasion		0	0	2	3
Depth of invasion	T1	2	0	0	0
	T2	0	7	1	0
	T3	0	0	0	4
Lymph node metastasis	N0	4	0	0	0
	N1	0	3	6	0
	N2	0	0	0	1
Distant metastasis	M0	5	3	2	1
	M1	0	0	1	2

The depth of tumoral invasion ranged from mucosal and submucosal limited tumors (T1) in two cases to muscularis propria invasion (T2) in

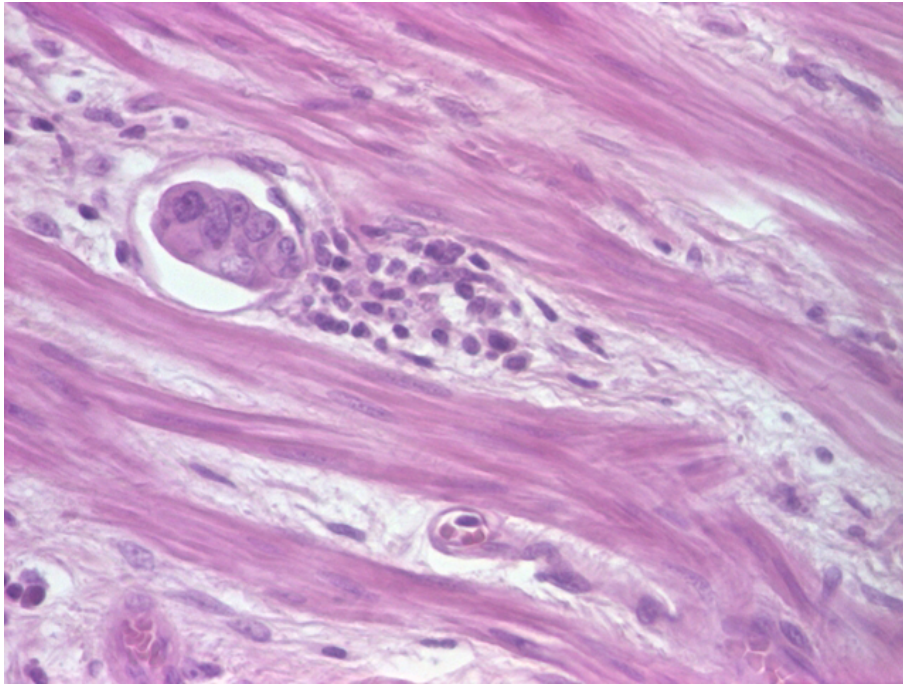
eight cases and adipose tissue invasion (T3) in five cases (Fig.3).



**Fig.3. High-grade tubular gastric carcinoma with the micropapillary component invading the muscular layer (T2), HE staining, x40**

We also observed the presence of lymphovascular neoplastic emboli in five cases of which two cases were tumors with the

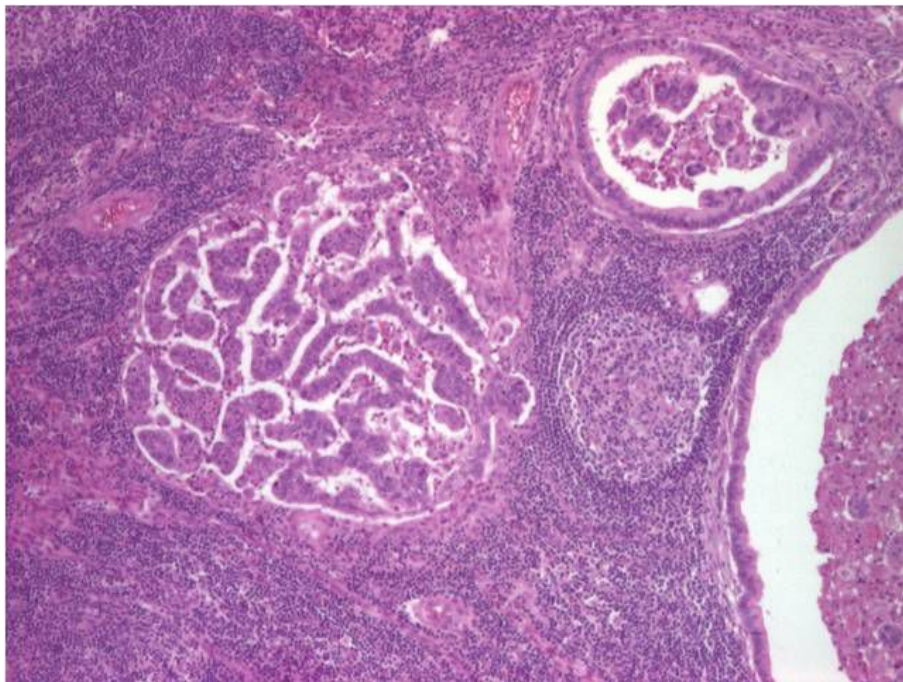
micropapillary component of 25-50% and three cases with more than 50% micropapillary component (Fig.4).



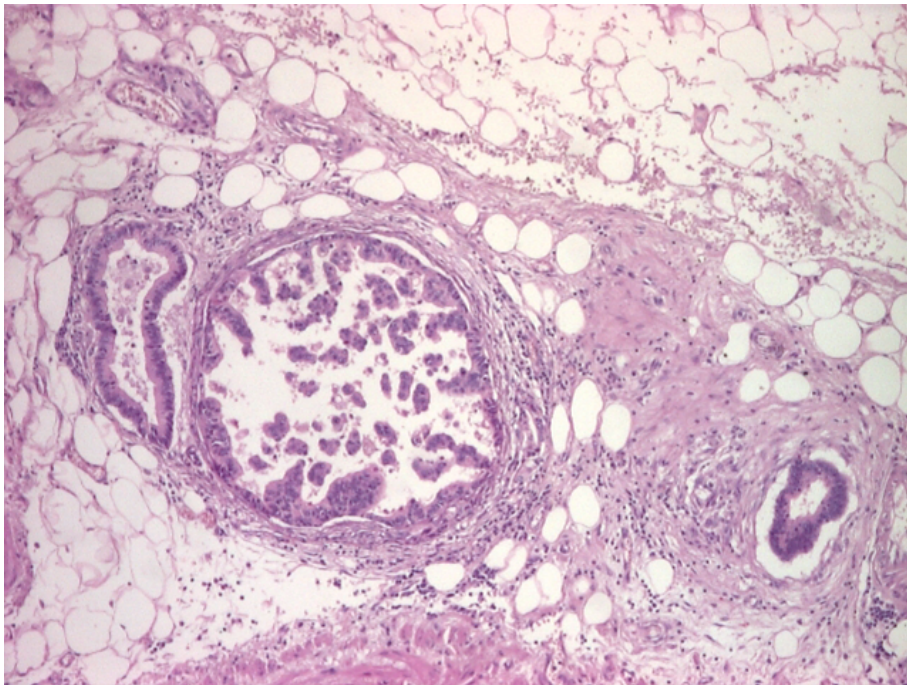
**Fig.4. Signet-ring gastric carcinoma with micropapillary component, lymph vessel invasion, muscular layer, HE staining x100**

The lymph nodes metastasis appeared in two cases only as micropapillary component and in the other case had the appearance of a mixture between tubular carcinoma and micropapillary

carcinoma (Fig.5). In two of the three cases of metastatic tumors, these were localized in epiploon in one case and in epiploon and liver in the others (Fig.6).



**Fig.5. Low-grade tubular gastric carcinoma with micropapillary component, lymph node invasion, HE staining, x40**



**Fig.6. Low-grade tubular gastric carcinoma with the micropapillary component invading the peritoneum, HE staining, x40**

## Discussions

Micropapillary carcinoma is an aggressive variant of adenocarcinoma with high incidence of lymphatic and distal metastasis, which hasn't been sufficiently studied for the stomach location. Gastric micropapillary carcinoma has recently been described by Shimoda et al. as an unusual type of gastric carcinoma [9].

Roh et al report a tumor incidence of up to 0.07% of the total of 15,254 subtotal gastrectomy specimens [12].

The mean age for diagnosis of this variant of gastric carcinoma is 66.2 years (36-87 years range), predominantly in males (male/female ratio: 2.5-3: 1). In the present study, the mean age of patients at the time of diagnosis was 64.3 years, also predominant in male gender.

No form of "pure" micropapillary carcinoma was found, all cases reported being combinations with tubular or papillary gastric adenocarcinoma.

In the 72 cases of micropapillary carcinomas analyzed by Eom et al., most tumors were combined with intestinal adenocarcinoma (88.9%) and papillary adenocarcinoma (59.7%), the rest being diffuse carcinomas (11.1%) and tubular adenocarcinomas (29.2%) [13].

Also, in the 14 cases we analyzed, the tumors were combined in seven cases with low-grade tubular carcinoma, in two cases with high-grade tubular carcinoma, in other two cases with

papillary carcinoma and in three cases with signet-ring carcinoma.

Although the invasive micropapillary component of gastric carcinomas is increasingly recognized as a distinct and aggressive variant, the diagnostic criteria remain quite imprecise. In addition, the threshold for the micropapillary carcinoma diagnosis based on the percentage/volume of the micropapillary component is undetermined, with no validated clinical-pathological data supporting the proportion of the micropapillary component in association with clinical outcome in these patients [14].

Roh et al. did not find significant clinical-pathological differences between the group with the micropapillary component  $\leq 20\%$  and the group with the micropapillary component  $> 20\%$  [12].

In our study, it varied between 5% and 90%. We found for low-grade tubular carcinomas that the association with the micropapillary component was present in less than 25%, for high-grade tubular carcinomas and papillary the association of the micropapillary component was between 25-50% and for the signet-ring 50%.

In some locations, such as the ovary and salivary glands, the micropapillary component was associated with a high incidence of lymph node metastasis and poor prognosis [5,15,16], while in other locations the prognostic

significance remains uncertain. In our study, the over 25% association of the micropapillary component was present in the carcinomas that invaded the entire gastric wall (T3), with lymphovascular emboli, lymph nodes metastasis or distal metastasis.

Literature data regarding the prognosis of gastric carcinomas with micropapillary component are limited and contradictory. While some studies report precisely an unfavorable prognosis [13], others consider that compared to other organs, the micropapillary carcinoma of the stomach does not have such a bad prognosis [12].

In the series reported to date, patients with micropapillary carcinoma had a global survival rate of 30% at 5 years, compared with 67% in patients with non-micropapillary carcinomas [12].

## Conclusions

Recognition of the micropapillary component in gastric carcinoma is critical because it is frequently associated with lymph node metastasis and worse prognosis.

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