

**Original contribution**

# The clinicopathological significance of micropapillary pattern in colorectal cancers<sup>☆,☆☆</sup>



Jung-Soo Pyo MD, PhD, Mee Ja Park MD, PhD<sup>\*</sup>, Dong-Wook Kang MD, PhD

Department of Pathology, Eulji University Hospital, Eulji University School of Medicine, Daejeon, Republic of Korea

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Prognosis

**Summary** The aim of the present study is to elucidate the clinicopathological significance and prognostic role of micropapillary pattern (MPP) in colorectal cancer (CRC). We investigated the correlation between the presence of MPP and clinicopathological characteristics and prognosis in 266 CRCs. In addition, the clinicopathological significance of MPP in mucin pools was investigated and compared to pure MPP, which is not associated with mucin pools. MPP, regardless of its proportion in the overall tumor, was found in 74 of 266 CRCs (27.8%). The rate of MPP in proportions  $\geq 5\%$  was 9.4% (25 of 266 cases). CRC with MPP showed higher rates of vascular and lymphatic invasion, higher metastatic lymph node ratio, and higher pT stage compared to CRC without MPP. In addition, increasing proportion of MPP in overall tumor showed more frequent vascular and lymphatic invasions ( $P = .002$  and  $P = .008$ , respectively). Among 74 CRCs with MPP, 25 CRCs were found in mucin pools (33.8%). These cases were more right-sided and poorly differentiated with less frequent lymphatic invasion and lymph node metastasis, compared to CRCs with pure MPP. The presence of MPP significantly correlated with worse overall survival ( $P = .010$ ). In 74 CRCs with MPP, overall survival significantly differed between pure MPP and MPP in mucin pools ( $P = .003$ ). Taken together, our data suggest that the presence of MPP significantly correlated with aggressive tumor behavior and worse survival in CRC. In addition, the clinicopathological significance of MPP in mucin pools differed from CRC with pure MPP.

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**1. Introduction**

Micropapillary features are defined as small cell clusters without fibrovascular cores locate in lacunar spaces [1-8]. Micropapillary carcinomas are described in various organs

such as breast, lung, ovary, and urinary bladder [9-11]. Micropapillary carcinoma is a rare variant in colorectal cancers (CRCs) [12]. However, adenocarcinoma with micropapillary pattern (MPP) is more frequent than pure micropapillary carcinoma in CRCs. In previous reports, MPP was found in 9.4% to 19.1% of CRCs [2,4,13-15]. In lung adenocarcinoma, MPP was found in 22.9% from a meta-analysis [16]. It is well known that micropapillary carcinoma has frequent lymphovascular invasion and lymph node metastasis [2]. Misreading histological characteristics of MPP may lead to misidentification of lymphovascular invasion because of confusion between lacunar and endothelial spaces. However, clinicopathological characteristics of CRCs with MPP are not fully

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<sup>\*</sup> Corresponding author at: Department of Pathology, Eulji University Hospital, Eulji University School of Medicine, 95 Dunsanse-ro, Seo-gu, Daejeon 35233, Republic of Korea.

E-mail address: pmj@eulji.ac.kr (M. J. Park).

understood, possibly because of the low incidence of MPP or micropapillary carcinoma.

The aim of the present study is to elucidate the clinicopathological significance and prognostic role of MPP in CRCs. To obtain the proper criterion for the proportion of MPP in the entire tumor, clinicopathological characteristics were evaluated by the proportion of MPP in CRCs. In addition, the clinicopathological significance and prognosis of cases with MPP in mucin pools were investigated.

## 2. Materials and methods

### 2.1. Patients

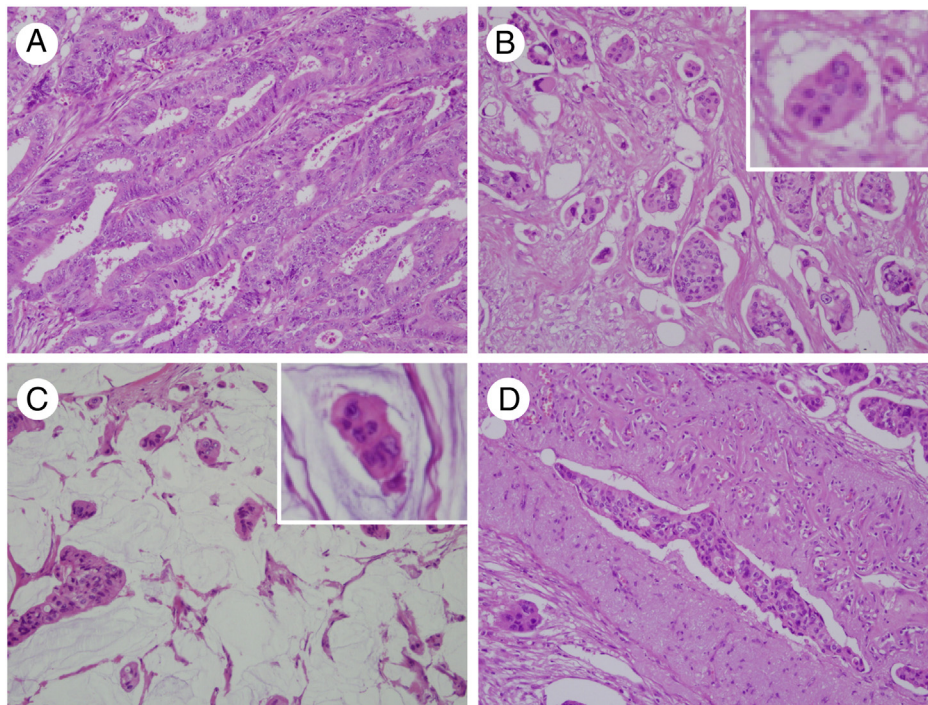
The files of 266 patients who had undergone surgical resection of CRCs in Eulji University Medical Center, Eulji University School of Medicine (Republic of Korea), from January 1, 2001 to December 31, 2010, were analyzed. We evaluated clinicopathological characteristics, such as the presence of MPP and mucin pools; age; gender; tumor size, location, differentiation, depth; vascular, lymphatic, and perineural invasion; lymph node metastasis, metastatic lymph node ratio, distant metastasis; and pathologic tumor-node-metastasis (pTNM) stages by reviewing medical charts, pathological records, and glass slides. This protocol was reviewed and approved by the Institutional Review Board of Eulji University Hospital (Approval No. EMC 2017–10-002).

### 2.2. Evaluation of micropapillary pattern

To elucidate the clinicopathological significance of MPP, the presence of MPP was investigated in 266 CRCs. MPP is characterized by (1) tumor cell clusters without fibrovascular cores, (2) tumor cells with pleomorphic nuclei and eosinophilic cytoplasm, and (3) location in stromal spaces, resembling lymphovascular spaces [2-8]. In some cases, MPP in mucin pools was identified. To evaluate the clinicopathological characteristics of MPP in mucin pools, CRCs with MPP were classified as either pure MPP or MPP in mucin pools. In the present study, the comparisons between CRCs with MPP and without MPP, and between pure MPP and MPP in mucin pools were conducted. Mucinous adenocarcinoma, which is composed of pools of extracellular mucin in >50% of the lesion, was not included in the present study.

### 2.3. Statistical analysis

Statistical analyses were performed using SPSS version 22.0 software (SPSS, Chicago, IL, USA). The significance of the correlation between the presence of MPP and the clinicopathological characteristics was determined by either the  $\chi^2$  test or the Fisher exact test (two-sided). The comparisons between the presence of MPP and age, tumor size, and metastatic lymph node ratio were analyzed using the two-tailed Student *t* test. Survival curves were estimated using the Kaplan–Meier product-limit method, and differences between the survival



**Fig. 1** Representative images showing immunoreactivity for micropapillary pattern in colorectal cancers ( $\times 400$ ). A, Adenocarcinoma without micropapillary pattern. B, Adenocarcinoma with micropapillary pattern. C, Adenocarcinoma with micropapillary pattern in mucin pools. D, Vascular invasion of micropapillary pattern.

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