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Original

Clinical Impact of Pathological Sub-classification for Colorectal Mucinous Adenocarcinoma

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Introduction: The mucinous nature of the tumor as a predictor of the prognosis remains controversial. Colorectal mucinous adenocarcinoma is counted as a risk factor for recurrence in cases of stage II colorectal cancer in ASCO2004 Guideline. The present study was undertaken to attempt pathological sub-classification of mucinous adenocarcinoma (MC) based on the presence/absence of poorly differentiated adenocarcinoma or signet ring cell carcinoma (PCC) components, and to evaluate the clinical significance of such sub-classification. **Materials and Methods:** The patients with stage II or stage III colorectal cancer who underwent radical surgery at our department between 1991 and 2005, 27 patients with MC and 831 patients with non-MC (NMC) were enrolled in this study. Subsequently, MC was pathologically sub-classified into MC containing a PCC (MCP) and MC not containing a PCC (MCNP). The clinicopathological factors, OS (overall survival) and RFS (relapse free survival) were analyzed by each subclass of MC. **Results:** There were 22 cases of MCP and 5 cases of MCNP. Percentage of stage III patients with lymph node metastasis was higher in the MCP as compared to that in the MCNP ($p = 0.047$). The RFS in the patients with stage II, MCP was associated with a poorer prognosis than MCNP + NMC (5-year RFS MCNP + NMC 87.3% vs. MCP 57.1% $p = 0.0117$). Multivariate identified three independent risk factors for recurrence: male gender, diagnosis of MCP, and vascular invasion (+). **Conclusion:** MCP carried a poorer prognosis as compared to NMC and MCNP. In patients with stage II, the diagnosis of MCP was identified as an independent risk factor for recurrence.

Key Words: colorectal mucinous adenocarcinoma, pathological sub-classification, prognostic factor

Introduction

Colorectal mucinous adenocarcinoma is a histological subtype of colorectal cancer that is characterized by extracellular formation of a macromolecular glycoprotein[1]. Its incidence is lower than that of well-differentiated or moderately-differentiated colorectal adenocarcinoma, this subtype of cancer accounting for 5-15% of all cases of colorectal cancer[1)~8)]. Clinicopathologically, this is seen relatively more frequently in younger individuals[4)9)10)] and in females[11)], shows a predilection for the right side of the colon[4)7)11)], and is often characterized by a large tumor diameter and large depth of invasion at diagnosis[7)12)]. While according to some reports, the prognosis of non-mucinous adenocarcinoma does not differ significantly from that of mucinous adenocarcinoma, other reports suggest a less favorable prognosis of the mucinous type of adenocarcinoma[1)2)4)6)11)]. The mucinous nature of the tumor as a predictor of the prognosis remains controversial. Mucinous adenocarcinoma is listed as a risk factor for recurrence in cases of stage II colorectal cancer in the American Society of Clinical Oncology (ASCO) 2004 Guideline[13)14)], and also as a condition

necessitating additional resection when dealing with submucosal (sm) cancer in Japan[12]. On the other hand, the AJCC (American Joint Committee on Cancer) does not recognize any sub-classification of colorectal mucinous adenocarcinoma or regard this cancer as being associated with a poor prognosis like that of poorly differentiated adenocarcinoma[14]. Mucinous adenocarcinoma is known to be classified as well differentiated mucinous adenocarcinoma and poorly differentiated mucinous adenocarcinoma in Japan[12]. Moreover, signet-ring cell carcinoma components are routinely seen in mucinous adenocarcinoma in actual clinical practice[5][6], but no reports have clarified whether the proportion of a mucinous adenocarcinoma occupied by the signet-ring cell carcinoma is reflected in the outcome.

The present study was undertaken to attempt pathological sub-classification of colorectal mucinous adenocarcinoma based on the presence/absence of poorly differentiated adenocarcinoma or signet ring cell carcinoma (PCC) components, and to evaluate the clinical significance of such sub-classification.

Materials and Methods

Of the patients with stage II or stage III colorectal cancer who underwent radical surgery at our department between January 1991 and December 2005, 27 patients with mucinous adenocarcinoma (MC) and 831 patients with non-mucinous adenocarcinoma (NMC) were enrolled in this study. MC was defined as colorectal cancer associated with an extracellular mucus volume in excess of 50% of the tumor volume, in accordance with the World Health Organization definition[15]. There were no significant differences in the gender distribution, age, tumor site, tumor size, proportion of cases with lymph node metastasis, proportion of cases with vascular invasion, serum carcinoembryonic antigen (CEA) level, pathological stage, history of adjuvant therapy, or the number of lymph nodes examined for metastasis between the MC and NMC groups. Analysis of the depth of invasion revealed a higher percentage of T4 cases in the MC group ($p = 0.002$) (Table 1). The median observation period of the study population was 62.4 months. Presence/absence of distant metastases was checked for by chest X-ray, whole-body CT, abdominal ultrasonography and intraoperative observation. For this study, the right side of the colon was defined as the colon segment proximal to the splenic curvature, while the left side of the colon was defined as the colon segment distal to the splenic curvature plus rectum. Patients who had received treatment with an oral 5-FU preparation for 6 months or longer were categorized into the "adjuvant therapy

Table 1 Patient's characteristics in all registered patients

Factors	MC	NMC	p
Gender			
Man	7 (26%)	494 (59%)	0.16
Woman	20 (74%)	337 (41%)	
Age at operation (year)			
<70	19 (70%)	544 (65%)	0.59
≥70	8 (30%)	287 (35%)	
Site of colorectal cancer			
Right	7 (26%)	261 (31%)	0.67
Left	20 (74%)	570 (69%)	
Maximam diameter of tumor			
<27 mm	0 (0%)	98 (12%)	0.05
≥27 mm	27 (100%)	733 (88%)	
Depth of invasion			
T3≥	11 (41%)	702 (84%)	0.002
T4	16 (59%)	129 (16%)	
Lymph node metastasis			
N (−)	11 (41%)	443 (53%)	0.24
N (+)	16 (59%)	388 (47%)	
Lymphatic invasion			
Ly (−)	6 (22%)	109 (13%)	0.16
Ly (+)	21 (78%)	722 (87%)	
Venous invasion			
V (−)	21 (78%)	583 (70%)	0.52
V (+)	6 (22%)	248 (30%)	
Preoperative serum CEA			
<4.8 ng/ml	18 (67%)	602 (72%)	0.50
≥4.8 ng/ml	9 (33%)	229 (28%)	
TNM stage			
II	11 (41%)	439 (53%)	0.24
III	16 (59%)	392 (47%)	
Adjuvant chemotherapy			
Yes	11 (48%)	273 (38%)	0.38
No	12 (52%)	452 (62%)	
Unknown	4	106	
Number of harvested lymph node			
<12	7 (26%)	250 (30%)	0.83
≥12	20 (74%)	581 (70%)	
Follow up period: median (months)	62.4 (7.2-135)	62.4 (2.1-247)	0.91

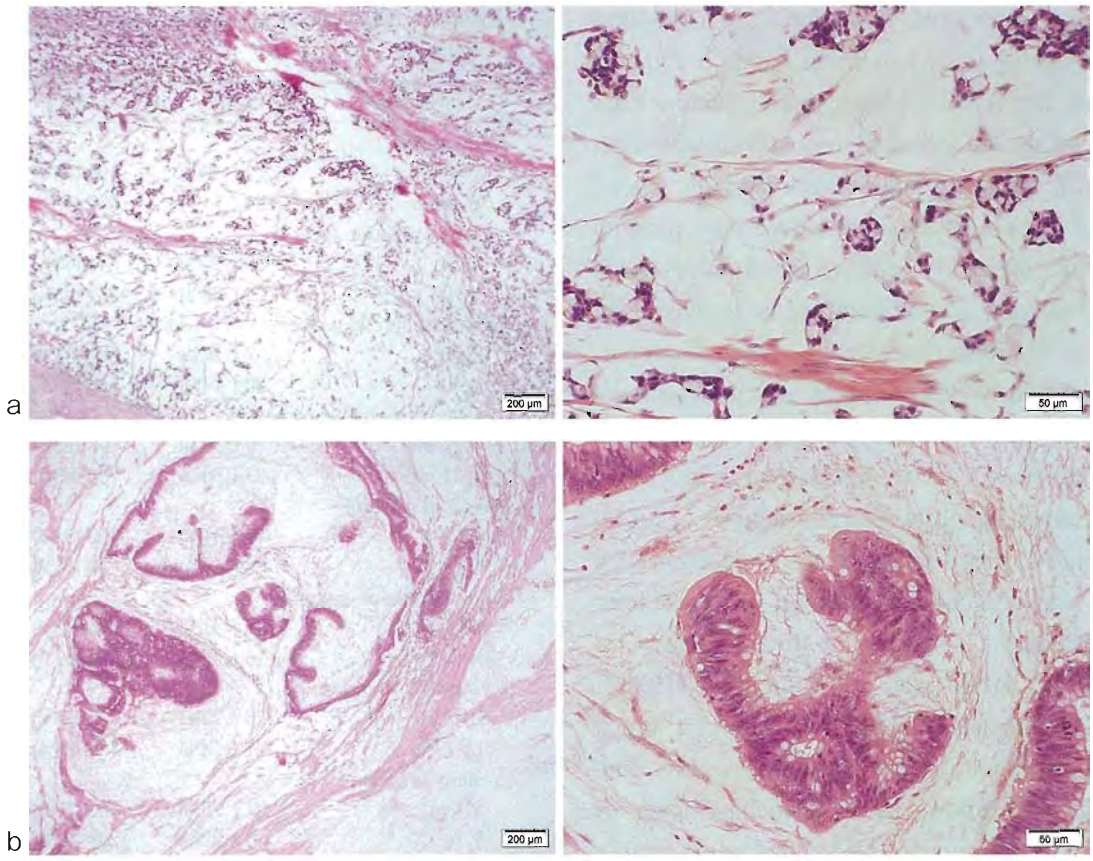

Fig. 1

a: MCP. Mucinous adenocarcinoma with poorly differentiated adenocarcinoma or signet ring cell carcinoma component.

b: MCNP. Mucinous adenocarcinoma with no poorly differentiated adenocarcinoma or signet ring cell carcinoma component.

present" group.

The overall survival rate (OS) and relapse-free survival rate (RFS) were compared between the patient groups with MC and NMC. Subsequently, MC was pathologically sub-classified into MC not containing a PCC component (MCNP, Fig. 1a) and MC containing a PCC component (MCP, Fig. 1b). This sub-classification was based on assessment of a full section of the main part of the tumor after 20% formalin fixation, paraffin embedding and hematoxylin-eosin staining of the resected surgical specimen. A single pathologist checked all the preparations and classified the cases of mucinous adenocarcinoma into 2 groups (MCNP and MCP) depending on whether the tumor contained a PCC component or not. The preparations as a whole was examined in 10-power fields, and after checked whether PCC was present in 20-power fields, if PCC was observed in one 20-power fields, the tumor was classified as MCP. Viable parts of the specimens were inspected, and parts of the tumor containing degenerating cells were not inspected. The clinicopathological factors, OS and RFS were analyzed by each subclass of MC. Furthermore, the prognosis of patients with each MC subclass was compared with that of the patients with NMC, accompanied by evaluation of the significance of the subclassification of MC by analysis of the incidence of tumor recurrence at different stages.

This clinical study was approved in advance by the Tokyo Women's Medical University Ethical Committee (Approval No. 2889).

Statistical analysis

Statistical analysis was performed by using a computer software program (JMP, SAS Institute, NC, USA version 10). Pearson's chi-square test was

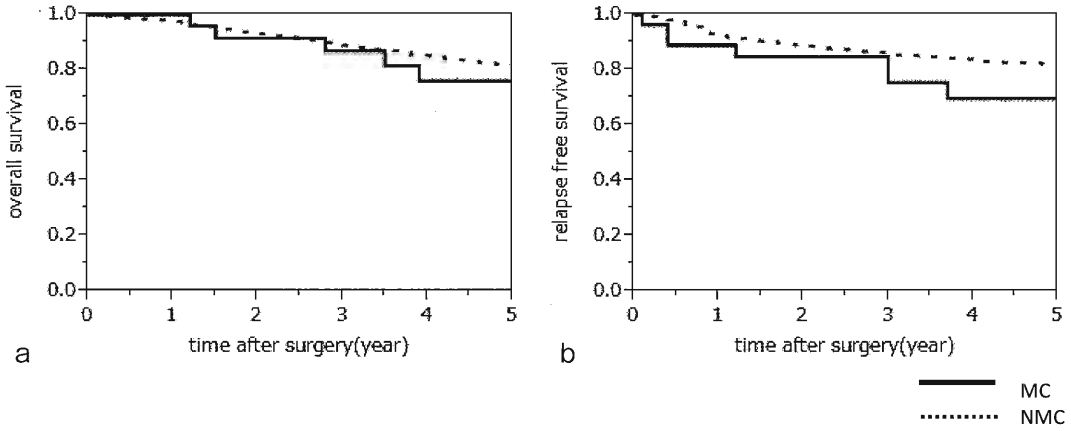

Fig. 2

a: Overall survival of patients with MC and NMC.
5-year survival: MC 70.6%, NMC 81.2%, p = 0.67.
b: Relapse free survival of patients with MC and NMC.
5-year survival: MC 63.8%, NMC 82.1%, p = 0.05.

used for two-variable analyses. The cutoff levels for the age, tumor size and serum CEA level were calculated from the respective receiver operating characteristic (ROC) curves. The Kaplan-Meier method was employed for analysis of the prognosis, followed by evaluation with the log-rank test. A Cox proportional hazards model was used for multivariate analysis and calculation of the risk ratio and 95% confidence interval. $P < 0.05$ was regarded as denoting statistical significance.

Results

1. Prognosis of MC and NMC

The 5-year OS and 5-year RFS were 70.6% and 63.8% in the MC group and 81.2% and 82.1% in the NMC group, respectively. Thus, there was no significant difference in the prognosis between the two groups, although the RFS tended to be slightly poorer in the MC group (Fig. 2a, 2b).

2. Prognosis analyzed by the MC subclass

There were 22 cases of MCP (81.5%) and 5 cases of MCNP (18.5%).

Evaluation of the clinicopathological factors by the MC subclass revealed no significant differences in the gender distribution, age, tumor site, depth of invasion, proportion of patients with vascular invasion, serum CEA level, history of adjuvant therapy, or the number of lymph nodes examined. The percentage of stage III patients with lymph node metastasis was significantly higher in the MCP group (15 cases, 68%) as compared to that in the MCNP group (1 case, 20%) (p = 0.047, Table 2).

The 5-year OS and 5-year RFS were both 100% in the MCNP group, while they were 70.9% and 55.7%, respectively, in the MCP group. Thus, MCP tended to be associated with a poorer prognosis as compared to MCNP, although the difference was not statistically significant (Fig. 3a, 3b).

3. Comparison between each MC subclass and NMC

The 5-year OS was 70.9%, 100% and 81.2% in the MCP group, MCNP group and NMC group, respectively. The 5-year RFS in the three groups was 55.7%, 100% and 82.1%, respectively (Fig. 4a, 4b). Thus, both the OS and RFS tended to be poorer in the patients with MCP than in those with MCNP or NMC (MCP vs NMC OS p = 0.35, RFS p = 0.007) (MCNP vs NMC OS p = 0.36, RFS p = 0.35). When this comparison was made between patients with MCP and MCNP + NMC, the RFS was significantly poor in the patients with MCP (5-year RFS MCNP + NMC 82.2% vs MCP 55.7% p = 0.0070) (Fig. 5b).

In the analysis of the RFS in the patients with stage II disease, MCP was associated with a significantly poorer prognosis than MCNP + NMC (5-year RFS MCNP + NMC 87.3% vs MCP 57.1% p = 0.0117)

Table 2 Patient's characteristics in all mucinous carcinoma

Factors	MCNP	MCP	p
Gender			
Man	4 (80%)	16 (72%)	0.73
Woman	1 (20%)	6 (27%)	
Age at operation (year)			
<70	4 (80%)	15 (68%)	0.60
≥70	1 (20%)	7 (32%)	
Site of colorectal cancer			
Right	2 (40%)	5 (23%)	0.42
Left	3 (60%)	17 (77%)	
Maximam diameter of tumor			
<27 mm	0 (0%)	0 (0%)	0
≥27 mm	5 (100%)	22 (100%)	
Depth of invasion			
≤T3	2 (40%)	9 (41%)	0.97
T4	3 (60%)	13 (59%)	
Lymph node metastasis			
N0	4 (80%)	7 (32%)	0.04
N (+)	1 (20%)	15 (68%)	
Lymphatic invasion			
Ly (−)	3 (60%)	4 (18%)	0.05
Ly (+)	2 (40%)	18 (82%)	
Venous invasion			
V (−)	5 (100%)	16 (73%)	0.18
V (+)	0 (0%)	6 (27%)	
Preoperative serum CEA			
<4.8 ng/ml	5 (100%)	13 (59%)	0.07
≥4.8 ng/ml	0 (0%)	9 (41%)	
TNM stage			
II	4 (80%)	7 (32%)	0.04
III	1 (20%)	15 (68%)	
Adjuvant chemotherapy			
Yes	1 (25%)	9 (47%)	0.57
No	3 (75%)	10 (53%)	
Unknown	1	3	
Number of harvested lymph node			
≥12	2 (40%)	5 (23%)	0.42
<12	3 (60%)	17 (77%)	

(Fig. 6a). In the analysis of the RFS among the patients with stage III disease, the prognosis did not differ significantly between the two groups (5-year RFS MCNP + NMC 76.7% vs MCP 53.2% p = 0.206) (Fig. 6b). Univariate analysis of the patients with stage II disease revealed a significant difference in the prognosis depending on the gender, presence of MCP or MCNP + NMC, and presence/absence of venous invasion (Table 3). Multivariate analysis, carried out including the factors identified by univariate analysis as having a significant influence, identified three independent risk factors for recurrence: male gender, diagnosis of MCP, and v (+) (Table 3).

Discussion

Colorectal mucinous adenocarcinoma is a histological subtype of colorectal cancer. While some reports suggest the absence of any significant difference in the prognosis between patients with mucinous and non-mucinous adenocarcinoma, others suggest a less favorable prognosis in patients with mucinous adenocarcinoma. Thus, the clinical significance of "mucinous" nature of the tumor as a prognostic factor is controversial. We undertook the present study based on our suspicion that patients with mucinous adenocarcinoma consist of a good prognosis group and a poor prognosis group. In the present study, assessment was based on observation of a full section of the main part of the tumor after the routine staining procedure (hematoxylin-eosin staining). When MC was sub-classified into MCP and MCNP, it was found that MCNP was associated with a better prognosis and that MCP was associated with a poorer prognosis than NMC and MCNP. Particularly in patients with stage II disease, detection of MCP was shown to be a useful prognostic factor.

Colorectal mucinous adenocarcinoma has been reported to account for about 5-15% of all cases of colorectal cancer[1)~8)]. As compared to the usual differentiated colorectal cancer, mucinous adenocarcinoma affects the right side of the colon more frequently[4)7)11)] and has a larger diameter at diagnosis as compared to the usual differentiated type of colorectal cancer. Furthermore, the depth of tumor invasion is frequently greater and the incidence of peritoneal metastasis is higher in cases of colorectal mucinous adenocarcinoma[7)8)].

In the present study of patients with stage II and III disease who had undergone radical surgery at our facility, there were no significant differences in the gender ratio, age or distribution of the tumor site between the patient groups with mucinous and non-mucinous adenocarcinoma, however, the depth of invasion was significantly greater in the cases of mucinous adenocarcinoma.

Analysis of the prognosis of colorectal mucinous adenocarcinoma revealed no significant difference in the OS or RFS between the patients with muci-

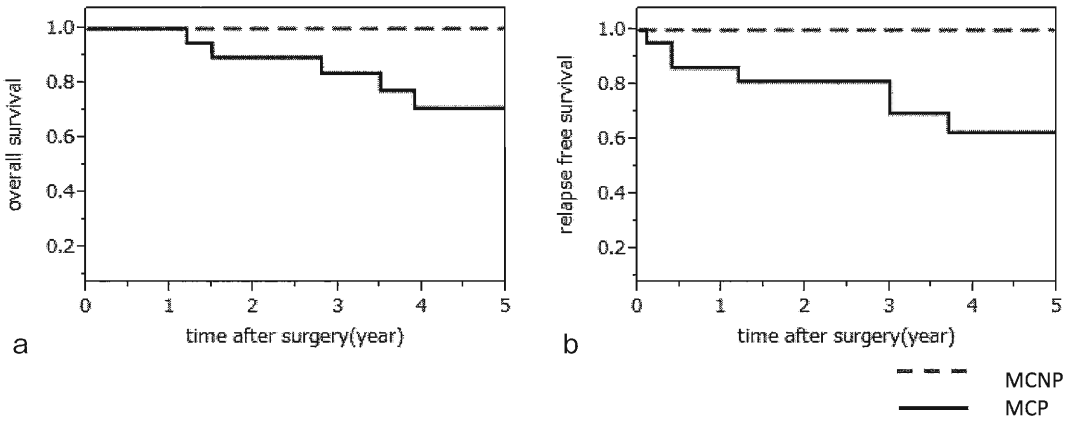

Fig. 3

a: Overall survival of patients with MCNP and MCP
5-year survival: MCNP 100%, MCP 70.9%, p = 0.27.
b: Relapse free survival of patients with MCNP and MCP
5-year survival: MCNP 100%, MCP 55.7%, p = 0.13.

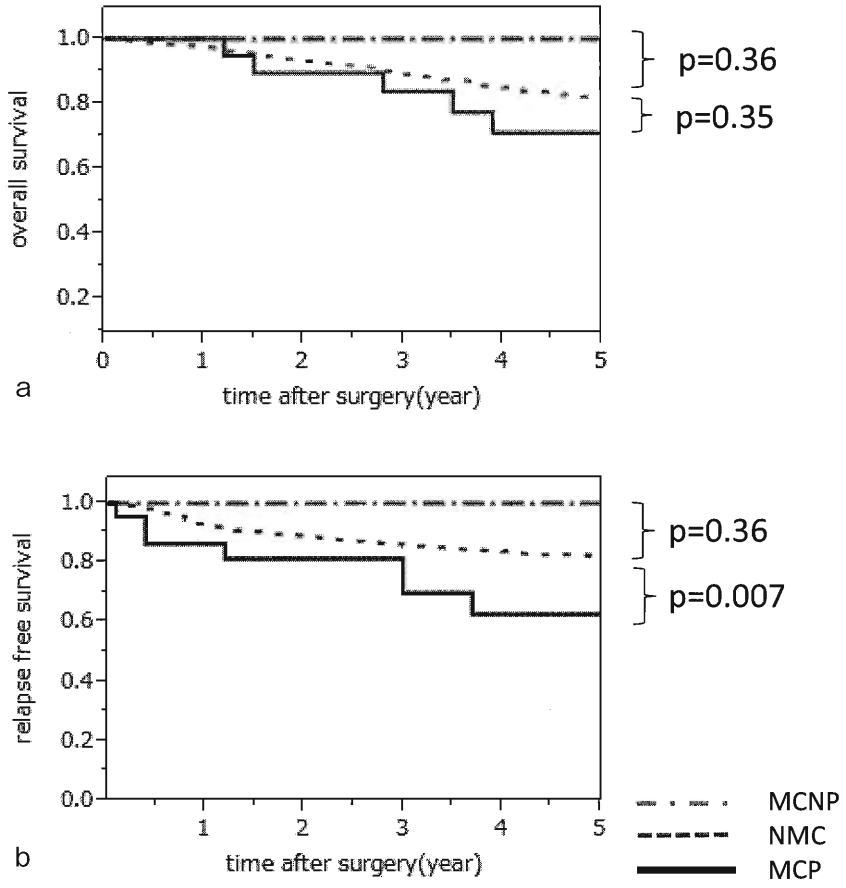

Fig. 4

a: Overall survival of patients with MCNP, MCP and NMC.
5-year survival: MCNP 100%, MCP 70.9%, NMC 81.2%.
b: Relapse free survival of patients with MCNP, MCP and NMC.
5-year survival: MCNP 100%, MCP 55.7%, NMC 82.1%.

nous and non-mucinous adenocarcinoma. Consistent with this result, Catalano et al also reported the non-inferiority of the prognosis of mucinous adenocarcinoma as compared to that of non-mucinous

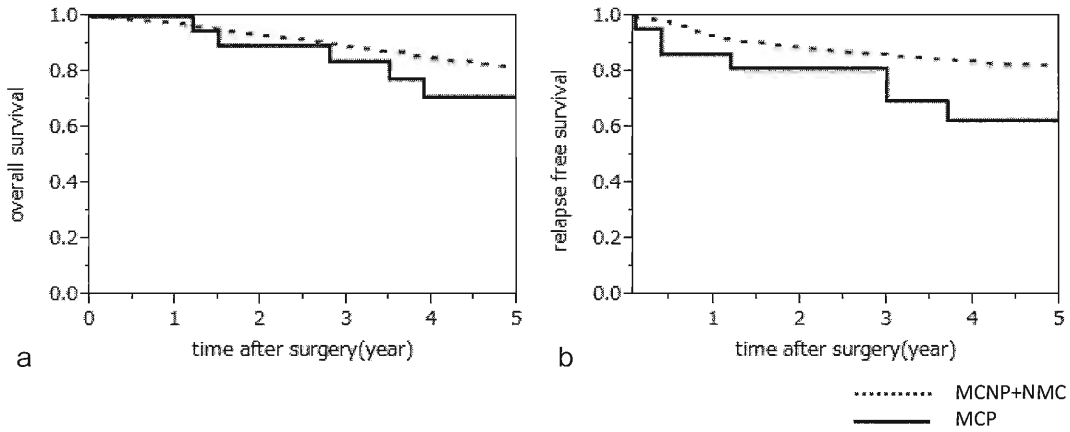

Fig. 5

a: Overall survival of patients with MCNP + NMC and MCP.
5-year survival: MCNP + NMC 81.4%, MCP 70.9%, p = 0.34.
b: Relapse free survival of patients with MCNP + NMC and MCP.
5-year survival: MCNP + NMC 82.2%, MCP 55.7%, p = 0.007.

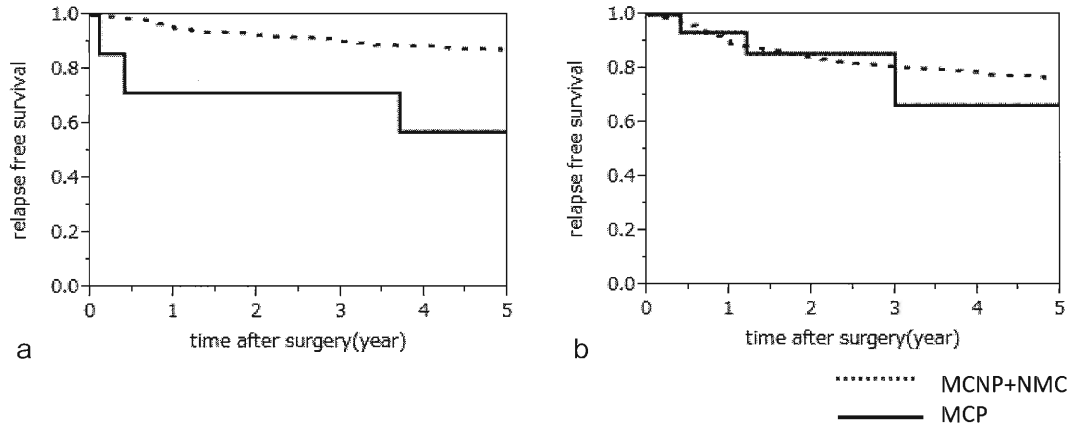

Fig. 6

a: Relapse free survival of patients with MCNP + NMC and MCP of stage 2.
5-year survival: MCNP + NMC 87.3%, MCP 57.1%, p = 0.01.
b: Relapse free survival of patients with MCNP + NMC and MCP of stage 3.
5-year survival: MCNP + NMC 76.7%, MCP 53.2%, p = 0.20.

adenocarcinoma bases on an analysis of colon cancer patients who had undergone radical surgery[5]. On the other hand, another report, based on an analysis of T3N0 colonic cancer patients who had undergone radical surgery, indicated that mucinous adenocarcinoma was associated with a poorer prognosis, akin to that of poorly differentiated adenocarcinoma[16].

The definition of non-mucinous adenocarcinoma varies among different reports published until date. Some reports count poorly differentiated adenocarcinoma as non-mucinous adenocarcinoma, while others do not adopt such a classification. Among the reports that count poorly differentiated adenocarcinoma as non-mucinous adenocarcinoma, some reports have indicated the prognosis is similar between patients with mucinous and non-mucinous adenocarcinoma[4)7)], while others suggest a more favorable prognosis in patients with mucinous adenocarcinoma than in those with non-mucinous adenocarcinoma[17].

Similarly, among the reports not counting poorly differentiated adenocarcinoma and signet ring cell carcinoma as mucinous adenocarcinoma, some have indicated a poorer prognosis in patients with mucinous adenocarcinoma as compared with that in pa-

Table 3 Univariate analysis of patient and tumor factors with 5-year relapse free survival in patients of stage II

Factors	n	5-year RFS (%)	p	Hazard ratio (95%CI)
Gender				
Man	288	83.1	0.004	Man/Woman
Woman	162	93.0		2.56 (1.34-5.41)
Age at operation (year)				
<70	287	84.6	0.16	
≥70	163	90.9		
Site of colorectal cancer				
Right	155	88.6	0.53	
Left	295	85.5		
Maximam diameter of tumor				
<27 mm	39	92.7	0.17	
≥27 mm	411	86.1		
Depth of invasion				
≤T3	385	87.7	0.38	
T4	65	86.1		
Lymphatic invasion				
Ly (−)	108	92.3	0.11	
Ly (+)	342	84.9		
Venous invasion				
V (−)	348	78.0	0.01	V (+)/V (−)
V (+)	102	89.3		2.09 (1.16-3.69)
Preoperative serum CEA				
<4.8 ng/ml	331	88.4	0.11	
≥4.8 ng/ml	119	82.0		
Adjuvant chemotherapy				
Yes	113	84.8	0.77	
No	289	88.2		
Unknown	48			
Number of harvested lymph node				
≥12	306	88.2	0.35	
<12	144	83.6		
Mucinous subclassification				
MCP	7	57.1	0.01	MCP/MCNP + NMC
MCNP + NMC	443	87.3		5.08 (1.21-14.2)

tients with non-mucinous adenocarcinoma [2)8)16)], while others have suggested a similar prognosis between the two types of cancer[9)14)18)]. J Verhulst et al reported that the risk ratio for recurrence was 2-8% higher in patients with mucinous adenocarcinoma than in those with non-mucinous adenocarcinoma, although the report did not clearly state whether poorly differentiated adenocarcinoma was counted as non-mucinous adenocarcinoma[11)].

While there are reports of sub-classification of mucinous adenocarcinoma depending on the presence/absence of a signet ring cell carcinoma component[19)~22)], no such sub-classification has been proposed by the WHO or AJCC[14)15)]. Furthermore the relationship between the sub-classes of cancer and the prognosis also remains unknown[22)23)]. In the present study, the assessment was based on observation of full sections of the main parts of the tumors after hematoxylin-eosin staining (a staining technique routinely used in clinical practice). Of the 27 cases of MC, 22 were rated as MCP, and the percentage of cases with lymph node metastasis was significantly higher in the MCP group than that in the MCNP group. The prognosis (OS and RFS) tended to be less favorable for MCP than for MCNP, although the differences were not statistically significant. This could be an underestimate due to the insufficient sample size. Evaluation of the prognosis by the subclass revealed that MCNP was associated with a poor prognosis and that MCP was associated

with a poorer prognosis as compared to NMC and MCNP. In this connection, it has been reported that mucinous colorectal carcinoma containing a signet ring cell carcinoma component carried a poorer prognosis than mucinous adenocarcinoma not containing such a component[19)21)]. In regard to the relationship between mucinous adenocarcinoma and signet ring cell carcinoma, the WHO and AJCC consider signet ring cell carcinoma and mucinous adenocarcinoma as independent entities[6)]. Thus, mucinous adenocarcinoma itself is viewed as an ambiguous prognostic factor whose significance remains unclear[22)].

Onodera et al reported differences from the molecular viewpoint between mucinous adenocarcinoma containing poorly differentiated adenocarcinoma and signet ring cell carcinoma components (MUC5AC-positive) and mucinous adenocarcinoma containing well-differentiated adenocarcinoma and moderately differentiated adenocarcinoma components (MUC1-positive). In addition, they also reported the existence of molecular similarities between the two types of mucinous adenocarcinoma (MUC2-positive and MUC6/MUC10-negative)[22)].

In the analysis of the RFS by the cancer stage, the prognosis of patients with stage II cancer was significantly poorer for MCP as compared to that for MCNP + NMC. Thus, the mucinous nature, or "MCP", was useful as a prognostic factor for determining a high risk of recurrence. To date, various sets of guidelines have been proposed concerning the risk factors for recurrence in patients with stage II disease, however, mucinous cancer is not listed under such factors[14)24)25)]. In the present study of patients with stage II colorectal cancer who had undergone radical surgery, multivariate analysis identified the diagnosis of MCP as a risk factor for recurrence. This is a new finding not reported before.

The percentage of cases of mucinous adenocarcinoma among all cases of colorectal cancer was rather low (3.1%) in the present study. To enable a statistically powerful analysis despite such a small sample size, individual cases were followed up for many years. For this reason, factors such as changes over time of the form of treatment could not be sufficiently excluded from the analysis, constituting a limitation of this study. In addition, the retrospective data analysis also constituted a limitation of the study. It is necessary in the future to analyze a larger number of cases, because the number of cases allocated to each subclass of mucinous adenocarcinoma was very small in the present study. Although we planned to consider analysis of the percentage of cases with the PCC component, this was not possible due to the small sample size. It is necessary in the future to evaluate the influence of the percentage of the PCC component on the prognosis. Because this sub-classification is relatively simple, inter-examiner errors are unlikely to occur when multiple pathologists are involved in the subclassification of the cases, however, it would be desirable to perform a validation study on the differences in the judgment in regard to the subclassification among different pathologists.

The association of mucinous adenocarcinoma with colitic cancer (secondary to inflammatory colon disease) and HNPCC (hereditary nonpolyposis colorectal cancer) has been a subject of debate[6)25)26)]. Walsh et al reported that mucinous adenocarcinoma was seen in HNPCC developing from serrated adenoma, pointing out the influence of the expression of MUC2, MUC5AC and MUC6 on carcinogenesis and the involvement of CpG island methylator activation and chromosome 11p15.5 in the development of the cancer[25)]. In the future, it would be desirable to clarify the differences in the cancer growth and progression patterns between MCP and MCNP from multiple viewpoints.

Conclusions

The clinical significance of sub-classification of mucinous adenocarcinoma was evaluated. Our findings revealed no difference in the prognosis between MC and NMC. However, after subclassification, MCNP was shown to have a better prognosis, while MCP carried a poorer prognosis as compared to NMC and MCNP. In patients with stage II disease, the diagnosis of MCP was identified as a significant independent risk factor for recurrence.

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The authors declare that they have no conflict of interest.

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大腸粘液癌における病理学的亜分類の臨床的意義

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〔はじめに〕大腸粘液癌は臨床的にはcontroversialな予後予測因子として扱われている．しかし，ASCO 2004 guidelineではstage II大腸癌の再発危険因子としてあげられている．本研究では粘液癌における非充実型低分化腺癌，印環細胞癌に由来する成分(mucinous adenocarcinoma oriented with poorly differentiated adenocarcinoma or signet ring cell carcinoma component：PCC)を含むか否かに着目して病理学的に亜分類を行い，この臨床的意義を明らかとすることを目的とした．〔方法〕教室で経験した1991年1月～2005年12月までのstage II，III根治手術症例のうち粘液癌（MC）27例と非粘液癌（NMC）831例を対象とした．PCCを含むMC（MCP）とPCCを含まないMC（MCNP）に病理学的に亜分類（MC sub-classification）を行った．MC sub-classification別に臨床病理学的因子，OS（全生存率）およびRFS（無再発生存率）について比較検討し，意義について検討した．〔結果〕リンパ節転移陽性，stage IIIの割合はMCNP1例(20%)，MCP15例(68%)とMCPが有意に多かった(p＝0.047)．stage IIでのRFSはMCPがMCNP＋NMCより有意に予後不良であった（5-year RFS MCNP＋NMC 87.3% vs MCP 57.1% p＝0.0117)多変量解析では男性，MCP，脈管侵襲陽性が独立した再発リスク因子として確認された．〔結論〕MCNPは予後良好であり，MCPはNMCおよびMCNPに比べて予後不良であることが判明した．さらにstage IIにおいてMCPは独立して有意な再発リスク因子であった．