Clinicopathological Characteristics of Mucinous and Non-Mucinous Adenocarcinoma in the Colon and Rectum in Rajavithi Hospital, Thailand

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Background: *The clinicopathological characteristics of colorectal mucinous adenocarcinoma (MA) are still controversial. Most of the reports suggested that MA were associated with worse clinicopathological behavior and poorer prognosis than non-mucinous adenocarcinoma (NMA) while the others showed no difference.*
Objective*: To compare clinicopathological characteristics and tumor recurrence of MA patients with those in NMA patients.*
Material and Method: *During the period of 2000 to 2009 in Rajavithi Hospital, a total of 427 colorectal adenocarcinoma patient records consisting of 407 NMA and 20 MA were included in this study. Mean age, tumor location, TNM staging at diagnosis, T- stage, N-stage, preoperative CEA level and recurrent rate of MA patients were compared with those of NMA patients.*
Results*: The distribution of MA patients for gender, mean age, tumor location, TNM stage and preoperative CEA level were similar to those of NMA patients (all p > 0.05). Only the tumor recurrence in MA was significantly more common than that in NMA (p = 0.020, OR = 3.28 (1.14-9.43)), whereas the TNM stage was not significantly different from NMA (p = 0.530). The metastatic site and pattern of metastasis also showed no statistical significance (p = 0.125).*
Conclusion*: The prognosis of MA is poorer than NMA. This may be associated with mucinous histological type itself.*

Keywords*: Colorectal mucinous adenocarcinoma, Mucinous carcinoma of colorectum, Colorectal mucinous carcinoma, Colorectal carcinoma.*

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Colorectal cancer (CRC) is the forth most common cancer in Thailand. The incidence of CRC is 11.3 per 100,000 males and 7.9 per 100,000 females[1]. Mucinous adenocarcinoma (MA) is one of the histological subtypes of colorectal cancer that comprises approximately 10-20% of all epithelial colorectal cancers in the West[2-5]. Most reports have suggested that MA affects young patients, involves with more proximal colon, presents in more advance stage, and has a poorer prognosis than NMA[2,4,5], while the other studies reported differently[6-8].

Material and Method

The study was approved by the Research Ethics Committee of the Rajavithi hospital. A retrospective study of colorectal adenocarcinoma patients treated by the author at Rajavithi Hospital between 2000 and 2009 were reviewed. There were 20 patients with MA and 407 patients with NMA. The other types of colorectal cancer such as GIST, carcinoid were excluded from the study. The mean age, gender, primary tumor location, TNM staging at diagnosis, preoperative CEA level, tumor recurrence and site of metastasis were obtained from medical records (Table 1).

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Definition

MA is characterized by extracellular mucin constituted more than 50% of the tumor volume by histological examination[9] (excluded signet ring colorectal cancer).

Tumor location

Right-sided colon-arising in the cecum,

Table 1. Data of colorectal adenocarcinoma patients

Factors	Mucinous (MA) n = 20	Non-mucinous (NMA) n = 407	p-value
Sex (M/F)			0.094
Male	15 (75.0)	228 (56.0)	
Female	5 (25.0)	179 (44.0)	
Age			
Mean ± SD	59.71 ± 12.79	58.70 ± 15.19	0.733[T]
Min-Max	22-81	20-87	
Location			0.567
Rectum	10 (50.0)	230 (56.5)	
Colon	10 (50.0)	177 (43.5)	
Right	6 (60.0)	51 (28.8)	0.070[F]
Left	4 (40.0)	126 (71.2)	
TNM staging (I, II, III, IV) 1			0.807[C]
I+II	8 (40.0)	192 (47.2)	
III	8 (40.0)	138 (33.9)	
IV	4 (20.0)	77 (18.9)	
TNM staging (I, II, III, IV) 2			0.530[C]
I+II	8 (40.0)	192 (47.2)	
III+IV	12 (60.0)	215 (52.8)	
Depth of invasion 1			0.480[C]
T1-T3	6 (30.0)	253 (37.8)	
T4	14 (70.0)	154 (62.2)	
Depth of invasion 2			0.091[F]
T1+T2	0 (0.0)	57 (14.0)	
T3+T4	20 (100.0)	350 (86.0)	
Lymph node involvement 1			0.532[C]
Present	11 (55.0)	187 (45.9)	
Absent	9 (45.0)	203 (49.9)	
Missing	0 (0.0)	17 (4.2)	
Lymph node involvement 2			0.245[F]
N0+N1	14 (70.0)	330 (81.1)	
N2	6 (30.0)	77 (18.9)	
Preoperative CEA level			0.884[C]
Normal	7 (35.0)	149 (36.6)	
Elevated	13 (65.0)	258 (63.4)	
Recurrence (Only stage 1,2,3)			0.020[F]*
No	10 (62.5)	279 (84.5)	
Yes	6 (38.5)	51 (15.5)	
Crude OR (95% CI) for Recurrence	3.28 (1.14-9.43)	1 (ref)	
Site of recurrence			0.125[F]
Loco-regional	3 (50.0)	10 (19.6)	
Distant (Liver, Lung)	3 (50.0)	41 (80.4)	

Values are represented as n (%), means ± SD and Min-Max, C = p-value from Chi-square test, F = Fisher exact test, T = Student t-test, * = Significant at $p < 0.05$

ascending colon, hepatic flexure, right side transverse colon.

Left-sided colon-arising in left side transverse colon, the splenic flexure, descending colon, sigmoid colon, rectosigmoid.

TNM Stage-according to the American Joint Committee on Cancer (AJCC) 6th, 2002[10].

Preoperative CEA level-normal range

0-3.4 ng/dL.

Statistical analysis

Chi-square test or Fisher exact test were used for comparing independent proportions. Student-t-test was used for comparing mean values. Disease free survival time was using Log Rank test. Statistical significance is defined as a p-value less than 0.05.

Results

The incidence of MA in the present study was 4.6% (20/407) of all colorectal adenocarcinoma. Male was predominant in both MA and NMA groups [75% (15/20) and 56% (228/407), respectively but there were no significant difference in gender between groups (p = 0.094). The mean age for patients diagnosed with MA and NMA were similar, 59.7 $\pm$ 12.79 years (range 22-81 years) and 58.7 $\pm$ 15.19 years (range 20-87 years), respectively (p = 0.733). The location of both MA and NMA groups were at similar distribution (p = 0.567) and the majority of tumors in both groups were located in the rectum. There were no significant differences in tumor stage between the two groups (p = 0.807) and also in advanced tumor stage (stage III + stage IV) (p = 0.530). Furthermore, there were no significant difference in the T_4 and N_2 categories (p = 0.480 and p = 0.245, respectively). Pre-operative CEA level was also similar in both groups (p = 0.884). Tumor recurrence in MA was significantly more common than that in NMA (p = 0.020, odds ratio with 95% confidence interval (OR) 3.28 (1.14-9.43)), whereas the metastatic site and pattern of metastasis were not statistically significant. Disease free survival at 2 years of NMA and MA were 87.70% vs. 70.91% (p = 0.003) (Fig. 1).

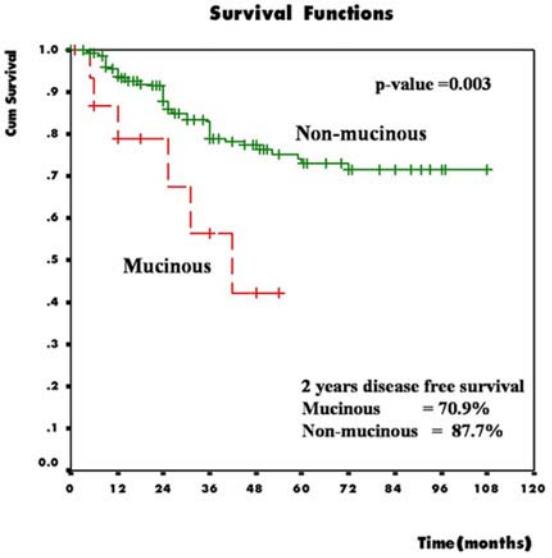

Fig. 1 Disease free survival of colorectal mucinous adenocarcinoma and Non-Mucinous and Mucinous

Discussion

Colorectal adenocarcinomas are derived from colonic epithelium and mainly are non-mucin producing cancer. The tumor cell that secrete mucin is classified as MA and signet ring cell adenocarcinoma, which are recognized as subtypes of colorectal cancer by the WHO[11] criteria. The clinicopathological significance of colorectal MA is controversial. Some studies have reported that MA affects younger patients[12], occurs more frequent in men[13,14] and has higher prevalence of elevated preoperative CEA levels. MA tumors are in advanced stage at diagnosis[4,15] and are more likely to invade adjacent viscera[16,17], thus involving extensive lymph node[17,18].

Disease recurrence in patients with MA[15] was more frequently observed than those with NMA and this might result in a poorer prognosis[19,20]. The others have reported no difference between groups[16,21]. It has been suggesting that, in addition to histological appearance, biological behavior in both groups also differs[8].

The data showed that the incidence of MA was 4.6%, similar to those in most Asian reports (approximately 2.9-7.4%)[16-18,22], but it was lower than those of the Western studies. Both MA and NMA patients were comparable in gender, mean age, tumor location, TNM stage and preoperative CEA level (all p > 0.1) except for tumor recurrence. The recurrence in MA group was significantly more common than that in NMA group, which is in agreement with most studies, while metastatic site and pattern of metastasis were similar in both groups. Disease free survival at 2 year of NMA was better than MA. Although MA patients showed higher rate of tumor recurrence, the TNM stage including cases with T4 (depth of invasion through serosa) and extensive node involvement (N2) in this group were not significantly different from those in NMA group.

Conclusion

The prognosis of MA is poorer than NMA, this may be associated with mucinous histological type itself.

Potential conflicts of nterest

None.

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การศึกษาลักษณะทางพยาธิคลินิกของผู้ป่วยมะเร็ง colorectal cancer ระหว่างชนิด mucinous adenocarcinoma กับ non-mucinous adenocarcinoma ในโรงพยาบาลราชวิถี

ไพบูลย์ จิวะไพศาลพงศ์, กัญญา บุญทองโท

ภูมิหลัง: มีรายงานการศึกษาบางฉบับพบว่าโรคมะเร็ง colorectal cancers ชนิด mucinous adenocarcinoma (MA) จะมีลักษณะโรคทางคลินิกที่แตกต่างและมีการพยากรณ์โรคที่มีความรุนแรงมากกว่ามะเร็งชนิด non-mucinous adenocarcinoma (NMA) แต่ก็มีรายงานการศึกษาบางฉบับที่มีผลการศึกษาแตกต่างจากรายงานข้างต้น

วัตถุประสงค์: เพื่อเปรียบเทียบลักษณะพยาธิคลินิกของโรคมะเร็งทั้ง 2 กลุ่มว่าจะมีลักษณะและความรุนแรงที่แตกต่างกันหรือไม่ ?

วัสดุและวิธีการ: ได้ทำการศึกษาผู้ป่วยที่รับไว้รักษาในโรงพยาบาลราชวิถีในช่วงระหว่างปี พ.ศ. 2543 ถึง พ.ศ. 2552 จำนวน 427 ราย โดยพบมะเร็งชนิด mucinous adenocarcinoma 20 ราย และ non-mucinous adenocarcinoma 407 ราย

ผลการศึกษา: มะเร็ง colorectal cancers ทั้ง 2 ชนิดนี้ ส่วนใหญ่จะมีลักษณะทางพยาธิคลินิกคล้ายคลึงกัน แต่กลุ่มผู้ป่วย mucinous adenocarcinoma จะมีอุบัติการณ์เกิดโรคซ้ำมากกว่า ($p = 0.020$) ซึ่งแสดงผลว่าการพยากรณ์โรครุนแรงมากกว่าแต่ตำแหน่งการเกิดโรคซ้ำรวมถึงระยะของโรคมะเร็งไม่แตกต่างกันทั้ง 2 กลุ่ม

สรุป: มะเร็งชนิด mucinous adenocarcinoma มีการพยากรณ์โรคที่รุนแรงกว่า ซึ่งอาจจะมีความสัมพันธ์กับสายพันธุ์