Survival of patients diagnosed with either colorectal mucinous or non-mucinous adenocarcinoma: A population-based study in Canada

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Abstract. Previous studies have shown conflicting results on the prognosis of colorectal mucinous adenocarcinoma. This study compared prognostic characteristics of patients diagnosed with mucinous and non-mucinous adenocarcinomas in a Canadian series. Analyses were based on 165 colorectal mucinous and 1215 non-mucinous adenocarcinoma patients who were registered at the Ottawa Regional Cancer Centre from 1994 to 1997, with follow-up extending to December 31, 2001. Differences in survival were examined using the relative survival analysis and the Cox proportional hazards model. For colon, rectum and both combined, the distribution for age at diagnosis, stage and treatment of patients with mucinous adenocarcinoma was similar to that of non-mucinous patients (all $p \geq 0.12$). Patients with mucinous histology had fewer well- or moderately-differentiated tumours than non-mucinous patients (all $p < 0.01$). Overall, no statistically significant differences were noted in 5-year relative survival between mucinous and non-mucinous carcinoma for colon, rectum and their combination ($p \geq 0.35$ for each). However, when the stages were considered separately, patients with stage III mucinous carcinoma had worse survival than patients with non-mucinous carcinoma for both sites. Multivariate analysis of combined data for colon and rectal cancers indicated that independent significant prognostic factors were stage for mucinous, with age and grade as well as stage for non-mucinous carcinoma. In conclusion, no significant differences in stage distribution and overall survival were found between mucinous and non-mucinous patients for colorectal cancer.

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Abbreviations: AJCC, American Joint Committee on Cancer; MA, mucinous adenocarcinoma; NMA, non-mucinous adenocarcinoma; ORCC, Ottawa Regional Cancer Centre; RSR, relative survival rate

Key words: colorectal cancer, histology, prognosis, relative survival rate, TNM stage, grade

Introduction

Colorectal cancer is a frequently diagnosed cancer in Canada and other industrialized countries (1,2). In Canada, colorectal cancer is currently the third leading cause of new cancer cases in men and women, and the second and third leading cause of cancer mortality among men and women, respectively (1). While mortality rates have been steadily declining over the last 20 years in the two genders, trends in incidence have been less significant, with slight fluctuations for men and modest decreases for women (1).

Mucinous adenocarcinoma (MA) is a histological subtype of colorectal cancer in which the neoplastic cells secrete abundant extracellular mucin within the infiltrating portion of the tumour (3). MA accounts for 10 to 20% of incident colorectal cancers in most Western series (4-6). While some studies have reported that patients with colorectal MA have a poorer prognosis than those with non-mucinous adenocarcinoma (NMA) (3,7-12), others have reported no difference (13-16). It has been suggested that, compared to the more common non-mucinous variety, MA tumours affect younger patients (17), have a greater propensity for early spread to regional lymph nodes (10) and are diagnosed at an advanced stage (17,18). They are less likely to be resected with negative margins (19) and have poorer response to chemotherapy relative to NMAs (20,21). Furthermore, previous studies showed that the difference in survival between MA and NMA was mainly related to the rectal locations (17), or to the stage III diseases (3,9,17). However, the American Joint Committee on Cancer concluded that histological tumour type was of no prognostic significance in patients with colorectal carcinoma (22).

The clinicopathological and prognostic significance of MA continues to be controversial. The lack of consensus may be attributable to the limited detection power inherent in studies that test small subsets of patients, to diversity in the inclusion of patients (e.g. different stage or grade diseases) and to disparity in the criteria for defining MA and NMA. Few studies have evaluated differences in survival between colorectal MA and NMA at the population level. Most of the

previous studies have been limited by a small number of incident MAs. Currently, little data are available in comparing prognostic factors between MA and NMA. To provide insights into the significance of mucinous histology in Canada, we compared 5-year relative survival rates and prognostic factors between colorectal MA and NMA based on data obtained from a population-based cancer registry in the Ottawa (Canada) region.

Materials and methods

Study population. Data were extracted for 1,460 cases of colorectal cancer [ICD-9 codes 153 and 154 (23)] registered by the Ottawa Regional Cancer Centre (ORCC) between 1994 and 1997. The ORCC covers all of Eastern Ontario and a part of Western Quebec and is the most complete census of cancer patients in the region. Patients were followed up to December 31, 2001 and their survival status was obtained through both active and passive follow-up, including record linkage with the Ontario Mortality Database. At the time of data analysis, we had survival information for 1,449 patients (824 deaths, 625 alive), while 11 (0.8%) were lost to follow-up. The median length of follow-up was 45 months. Patients living in the province of Quebec at the time of diagnosis were excluded from the analysis as they could not be linked to Ontario provincial mortality data.

Covariates included in the study were cancer site (colon and rectum), gender, age and stage at diagnosis, histological type, histological grade and treatment. Tumour stage at the time of diagnosis was coded using the TNM classification system (24). The TNM stage in these data was the pathological stage, augmented by the clinical stage when the pathological stage was not recorded. Age at cancer diagnosis was classified into 4 groups (<50, 50-59, 60-69, ≥70). Treatment was categorized as chemotherapy and/or radiotherapy, surgery only, surgery with chemotherapy, surgery with radiation and surgery combined with chemotherapy and radiation. The histological subtypes were classified using an established method defined by Berg (2,4,25,26) based on the ICDO-2 (27): MA, signet-ring cell adenocarcinoma, NMA, squamous cell carcinoma, undifferentiated carcinoma and other miscellaneous histology types. The histological grade is the degree of differentiation of the tumours: well-differentiated (G1), moderately-differentiated (G2), poorly-differentiated (G3) and those where the grade could not be assessed (Gx). As there were very few undifferentiated tumours (G4), they were combined with the poorly-differentiated tumours.

Statistical analysis. Patient characteristics at baseline for those with MA and NMA were compared using the Chi-square test, and differences in the mean age at diagnosis for men and women were examined using the t-test. All reported p-values were two-sided. Relative survival rates (RSRs) adjust for competing causes of death expected for persons in the general population of the same gender, age, period and geographic region as the colorectal cancer patients in the study, without requiring information on the actual cause of death of each patient. Relative survival analysis was performed by using a SAS macro program, in which the relative survival model

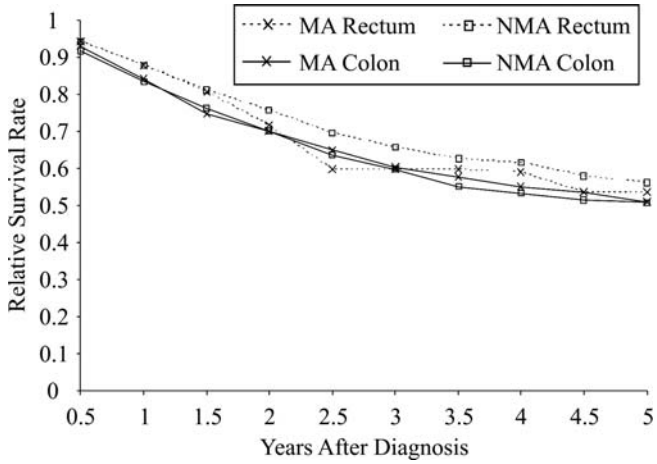

Figure 1. Relative survival rates for patients with mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA) of colorectum.

was estimated by a generalized linear regression with a Poisson error structure fitted to collapsed data based on exact survival time (28). The expected survival rates were derived by single year of age up to 109 from the gender-specific Ontario life table for the study period (29). The statistical significance of each covariate was assessed by the likelihood ratio test and Wald test, using the conventional level of 0.05. The goodness of fit for the models was evaluated on the basis of the deviance or the Pearson Chi-square statistic. The prognostic importance of gender, age, stage, histology and grade was analyzed by both univariate and multivariate Cox proportional hazards models. The assumption of proportionality was evaluated by inspecting plots of the log negative log survival curves and examining the statistical significance of time-dependent covariates in proportional hazard models.

Results

Of 1460 colorectal cancer patients, 65% (949) presented with colon cancer. MA accounted for 13% (124) of the colon cancer cases and 8% (41) of rectal cancer cases. The mean age for patients diagnosed with colon MA and NMA was similar (67 and 66 years, respectively, p=0.13). The corresponding figures among rectal patients were 65 and 65 years (p=0.71). The distribution of MA and NMA cases of colorectal cancer by study variables is shown in Tables I and II. For colon, rectum and both combined, the distribution for age at diagnosis, stage and treatment of patients with MA was similar to that of NMA patients (all p≥0.12). Colon MA patients were more likely to be female than NMA patients (p=0.04); whereas, incidence of both MA and NMA was greater among men than among women for rectum cancer (76% of MA and 67% of NMA) and the distribution was similar (p=0.26). The MA patients had fewer well-differentiated or moderately-differentiated tumours (colon 58 vs. 70%, rectum 54 vs. 72%) and more grade Gx cancers (colon 13 vs. 5%, rectum 20 vs. 7%) compared to the NMA patients (p<0.01 for each).

The 5-year RSR among MA and NMA colorectal cancer patients was 52 and 53%, respectively (Table III). Fig. 1 depicts the overall survival curves for colon or rectal MA and NMA patients across the 5-year span of follow-up. Overall, no

Table I. Distribution (number of patients and %) of mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA) cases of colon and rectal cancer by study variables.

	Colon cancer			Rectal cancer			Total		
Characteristics	MA	NMA	P-value[a]	MA	NMA	P-value[a]	MA	NMA	P-value[a]
Gender			0.04			0.26			0.09
Male	52 (41.9)	410 (52.1)		31 (75.6)	287 (67.1)		83 (50.3)	697 (57.4)	
Female	72 (58.1)	377 (47.9)		10 (24.4)	141 (32.9)		82 (49.7)	518 (42.6)	
Age at diagnosis (years)			0.24			0.89			0.30
<50	5 (4.0)	70 (8.9)		5 (12.2)	47 (11.0)		10 (6.1)	117 (9.6)	
50-59	21 (16.9)	146 (18.6)		6 (14.6)	81 (18.9)		27 (16.4)	227 (18.7)	
60-69	45 (36.3)	244 (31.0)		14 (34.2)	129 (30.1)		59 (35.8)	373 (30.7)	
70+	53 (42.7)	327 (41.6)		16 (39.0)	171 (40.0)		69 (41.8)	498 (41.0)	
Stage at diagnosis			0.42			0.86			0.43
I	7 (5.7)	50 (6.4)		6 (14.6)	72 (16.8)		13 (7.9)	122 (10.0)	
II	44 (35.5)	270 (34.3)		13 (31.7)	110 (25.7)		57 (34.6)	380 (31.3)	
III	42 (33.9)	214 (27.2)		12 (29.3)	129 (30.1)		54 (32.7)	343 (28.2)	
IV	27 (21.8)	209 (26.6)		5 (12.2)	73 (17.1)		32 (19.4)	282 (23.2)	
Unknown	4 (3.2)	44 (5.6)		5 (12.2)	44 (10.3)		9 (5.5)	88 (7.2)	
Grade			<0.01			<0.01			<0.01
G1	27 (21.8)	99 (12.6)		12 (29.3)	57 (13.3)		39 (23.6)	156 (12.8)	
G2	45 (36.3)	450 (57.2)		10 (24.4)	250 (58.4)		55 (33.3)	700 (57.6)	
G3 or G4	16 (12.9)	110 (14.0)		7 (17.1)	40 (9.4)		23 (13.9)	150 (12.4)	
Gx	16 (12.9)	35 (4.5)		8 (19.5)	31 (7.2)		24 (14.6)	66 (5.4)	
Unknown	20 (16.1)	93 (11.8)		4 (9.8)	50 (11.7)		24 (14.6)	143 (11.8)	
All	124 (13.6)	787 (86.4)		41 (8.7)	428 (91.3)	0.01[b]	165 (12.0)	1215 (88.0)	<0.01

[a]The p-value was calculated using a Chi-square test statistic to compare differences in the frequency distribution of the study variable between MA and NMA patients. [b]The p-value was calculated using a Chi-square test statistic to compare overall differences in the frequency distributions of MA and NMA between colon and rectum cancer patients.

Table II. Treatment[a] distribution (number of patients and %) of mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA) cases of colon and rectal cancer by stage.

	Colon cancer			Rectal cancer			Total		
Characteristics	MA	NMA	P-value[b]	MA	NMA	P-value[b]	MA	NMA	P-value[b]
Stage I and II			0.51			0.70			0.16
S	26 (51.0)	173 (54.1)		7 (36.8)	57 (31.3)		33 (47.1)	230 (45.8)	
S + C	18 (35.3)	85 (26.6)		2 (10.5)	15 (8.2)		20 (28.6)	100 (19.9)	
S + C + R	3 (5.9)	34 (10.6)		4 (21.1)	63 (34.6)		7 (10.0)	97 (19.3)	
Others[c]	4 (7.8)	28 (8.8)		6 (31.6)	47 (25.8)		10 (14.3)	75 (14.9)	
Stage III and IV			0.22			0.12			0.92
S + C	38 (55.1)	267 (63.1)		4 (23.5)	44 (21.8)		42 (48.8)	311 (49.8)	
S + C + R	7 (10.1)	51 (12.1)		11 (64.7)	87 (43.1)		18 (20.9)	138 (22.1)	
Others[d]	24 (34.8)	105 (24.8)		2 (11.8)	71 (35.2)		26 (30.2)	176 (28.2)	

[a]S, surgery; C, chemotherapy and R, radiotherapy. [b]P-value of Chi-square test. [c]Others include S+R, C +/R and no treatment. [d]Others include S only, S+R, C +/R and no treatment.

statistically significant differences between MA and NMA patients were observed for colon (p=0.87), rectum (p=0.35) and both combined (p=0.66, curves not shown), even though the RSR for rectal MA was slightly lower than for NMA. The 5-year RSRs for MA patients were further compared with those for NMA patients by gender, age, stage, grade and treatment for colon and rectal cancers separately and combined (Table III and Fig. 2). Differences in survival between MA

Table III. Comparison of 5-year relative survival rates (RSRs) [with 95% confidence intervals (CIs)] for patients with colorectal mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA) by gender, age at diagnosis, stage, grade and treatment.

	Colon				Rectum				Entire cohort			
	MA		NMA		MA		NMA		MA		NMA	
Characteristics	RSR	95% CI	RSR	95% CI	RSR	95% CI	RSR	95% CI	RSR	95% CI	RSR	95% CI
Total	51.0	40.4-60.7	50.7	46.7-54.7	53.5	35.2-68.8	56.1	50.4-61.4	52.3	43.0-60.7	52.6	49.3-55.7
Gender												
Male	43.5	27.5-58.5	50.9	45.2-56.4	54.4	32.6-71.8	59.3	52.3-65.7	49.1	35.7-61.3	54.4	49.9-58.6
Female	56.1	41.4-68.5	50.4	44.7-55.9	49.6	17.3-75.6	49.8	39.9-58.9	55.4	42.0-66.9	50.3	45.3-55.0
Age at diagnosis (years)												
<50	58.4	10.7-87.9	47.3	35.1-58.6	54.0	7.5-86.3	68.7	53.0-80.1	58.7	23.3-82.3	55.8	46.1-64.5
50-59	25.0	8.9-45.3	46.8	38.2-54.9	50.3	10.5-81.1	54.5	42.2-65.3	31.3	14.7-49.5	49.7	42.7-56.3
60-69	63.8	46.3-77.0	52.5	45.3-59.2	35.8	12.1-60.6	52.9	42.9-61.9	57.8	42.8-70.2	52.6	46.9-58.1
70+	47.6	29.1-64.0	52.4	45.2-59.1	69.1	29.5-89.4	54.6	44.0-64.0	54.4	37.3-68.7	53.1	47.2-58.7
Stage												
I	89.2	25.6-99.0	94.9	68.0-99.3	No deaths	-	92.3	77.6-97.5	93.9	48.9-99.4	95.5	81.3-98.9
II	79.5	56.6-91.2	78.5	71.4-84.0	68.6	32.2-88.2	62.0	49.4-72.3	80.0	59.4-90.9	74.5	68.4-79.7
III	44.9	27.7-60.6	56.4	48.3-63.7	32.9	8.8-60.2	57.3	47.2-66.0	43.2	28.2-57.3	57.0	50.8-62.8
IV	8.6	1.5-24.2	3.1	1.3-6.4	0.42	0.0-19.2	7.4	2.6-15.6	7.4	1.3-21.2	4.3	2.2-7.3
Grade												
G1	70.9	44.7-86.3	67.1	55.0-76.6	70.1	35.2-88.6	75.0	57.9-85.9	72.4	51.1-85.6	70.6	61.1-78.1
G2	44.5	27.1-60.5	56.5	51.0-61.5	59.1	23.9-82.5	58.5	50.9-65.3	48.8	32.8-63.0	57.2	52.8-61.3
G3 or G4	32.3	11.1-56.0	32.8	23.4-42.6	17.6	1.1-51.6	42.2	23.9-59.4	28.5	11.2-48.7	34.8	26.5-43.2
GX	48.8	21.1-71.8	19.5	7.8-34.9	52.4	10.4-83.1	32.5	15.1-51.3	52.1	28.0-71.6	24.8	14.5-36.6
Treatment[a]												
Stage I and II												
S	72.8	40.9-89.3	96.7	78.6-99.5	78.7	20.0-96.5	88.7	69.0-96.2	76.1	47.4-90.5	95.5	85.9-98.6
S + C	90.1	59.3-97.9	79.2	66.4-87.6	50.6	0.0-94.4	60.2	27.1-82.1	88.6	55.9-97.5	79.0	66.6-87.2
S + C + R	No deaths	-	38.3	20.4-56.1	74.7	11.7-96.1	70.6	54.3-82.0	85.9	31.7-98.0	59.8	47.0-70.4
Stage III and IV												
S + C	31.4	16.8-47.2	38.0	31.7-44.4	17.8	0.9-53.0	25.3	13.0-39.7	28.4	15.1-43.2	36.5	30.6-42.3
S + C + R	43.9	8.6-75.8	11.8	4.6-22.6	27.2	5.7-55.5	65.1	52.6-75.8	34.2	12.5-57.5	43.8	34.8-52.4

[a]Survival rates are presented in the table only for the most frequently used treatments. S, surgery; C, chemotherapy and R, radiotherapy.

Table IV. Univariate Cox proportional hazards analysis for colorectal mucinous adenocarcimoma (MA) and non-mucinous adenocarcinoma (NMA).

Variables	MA			NMA		
	Cases/Deaths	HR (95% CI)[a]	P-value	Cases/Deaths	HR (95% CI)[a]	P-value
Gender			0.69			0.55
Male	83/48	1.00		697/390	1.00	
Female	82/44	0.92 (0.61-1.39)		518/293	1.05 (0.90-1.22)	
Age at diagnosis (years)			0.23			0.01
<50	10/4	1.00		117/57	1.00	
50-59	27/18	2.59 (0.88-7.69)		227/119	1.18 (0.86-1.61)	
60-69	59/31	1.58 (0.56-4.47)		373/199	1.17 (0.87-1.57)	
70+	69/39	1.87 (0.67-5.23)		498/308	1.46 (1.10-1.93)	
Stage			<0.0001			<0.0001
I	13/2	1.00		122/21	1.00	
II	57/20	2.66 (0.62-11.36)		380/147	2.70 (1.71-4.26)	
III	54/33	5.34 (1.28-22.27)		343/179	3.99 (2.54-6.27)	
IV	32/30	24.57 (5.79-104.24)		282/274	23.05 (14.70-36.16)	
Unknown	9/7	9.76 (2.02-47.25)		88/62	6.89 (4.19-11.31)	
Grade			0.13			<0.0001
G1	39/15	1.00		156/62	1.00	
G2	55/32	1.75 (0.95-3.23)		700/358	1.45 (1.10-1.89)	
G3 or G4	23/17	2.51 (1.25-5.05)		150/107	2.85 (2.08-3.90)	
Gx	24/13	1.66 (0.79-3.49)		66/53	4.15 (2.88-5.99)	
Unknown	24/15	2.00 (0.98-4.09)		143/103	2.32 (1.70-3.19)	

[a]Hazard ratio (HR) and 95% confidence interval (CI).

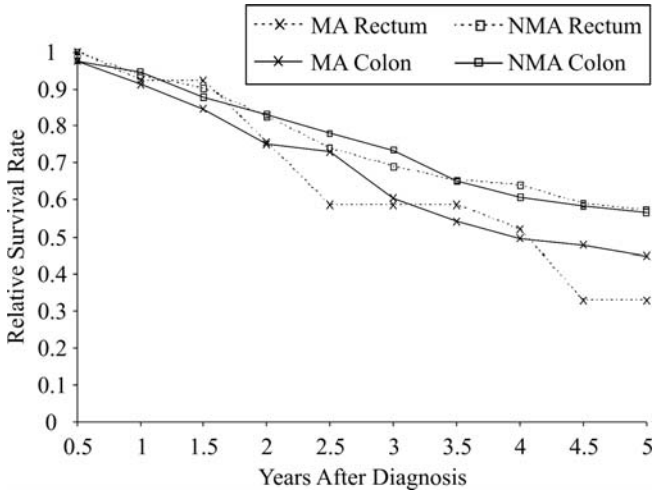

Figure 2. Relative survival rates for stage III colorectal cancer patients. MA, mucinous adenocarcinoma and NMA, non-mucinous adenocarcinoma.

and NMA were found in stage III disease for colon, rectum and their combination; survival was lower for MA compared to NMA (45 vs. 56% in colon, 33 vs. 57% in rectum and 43 vs. 57% for the combination). The RSR of MA was lower than NMA in patients aged 50-59 for colon and rectal cancers combined (31 vs. 50%). There were no differences in survival between MA and NMA patients with respect to gender and grade. For colon and rectal cancers combined, stage I and II NMA patients who were treated by surgery alone were more likely to survive than those who received other treatments; while, the MA patients who received surgery combined with chemotherapy were more likely to survive than those who received other treatments. Stage III and IV both NMA and MA patients who received surgery combined with chemotherapy and radiation had better survival rates than those who received surgery plus chemotherapy only.

When data for colon and rectal cancers were combined, univariate (Table IV) and multivariate analyses using the Cox model indicated that independent and significant prognostic factors were stage for MA, age, grade and stage for NMA.

Discussion

We observed that the prognosis of patients with MA occurring in the colon was similar to that of patients with NMA, whereas it was slightly worse for patients with MA occurring in the rectum (results did not reach significance) after multivariate analysis adjusted for age, gender, stage and grade. Stage was and remains the mainstay of prognostic classification of colorectal carcinoma. The similar distribution of stage between MAs and NMAs in our series, together with the fact that high levels of mucin secretion are less common in Western countries (30), may indicate a similar prognosis between MA and NMA. Du and his colleagues found that the RSR of patients with MA was similar to that of patients with NMA in the colon but

significantly lower in the rectum (17). In their Asian series, the proportion of MA in either colon or rectum was higher in advanced stages of the disease. The reason for this difference depending on location may be a manifestation of anatomic differences and surgical management. The lymphatic drainage of the pelvis is more extensive and varied compared with that of the abdominal colon and the ability to obtain wide lateral surgical margins within the pelvis is much more limited (8), thus leading to higher recurrence and metastatic rates and lower survival rates (8,19). Other authors (13-16) found that MA and NMA patients had a similar prognosis, even when outcome was compared by stage (14).

Overall, no statistically significant differences in survival were observed between MA and NMA for colon, rectum and both combined. However, when the stages were considered separately, patients with MA had worse survival than patients with NMA for stage III diseases of both sites; which is consistent with other studies (3,9,17). Furthermore, while the difference between NMA and MA in 5-year RSRs of patients with stage III disease was 12% for colon cancer, it was 24% for rectal cancer. This finding may contribute to the slightly lower overall RSR in patients with MA of the rectum compared with those with NMA. The survival difference between colon and rectal cancers in stage III disease can be explained by the percentage distributions of grade within stage III diseases: the higher ratio (1.8:1) of NMA-to-MA in well-differentiated or moderately-differentiated tumours in the rectum compared with a corresponding ratio of 1.4:1 for those in the colon. On the other hand, our study supports the notion that wide variation in survival within stages does exist, depending on such additional factors as grade. The histological grade of a tumour can supply prognostic information in addition to that provided by stage.

Our study confirms the most common clinical findings. MA accounted for 11% of colorectal cancer (colon, 13%; rectum, 8%). This prevalence is the same as those described in other studies (9,31) and corresponds to the reported range of between 10 and 20% in most Western series (4-6). The higher incidence of colorectal MA in the Ottawa region and in other Western countries, as compared with the incidence in some Asian countries (4%) (11,17), would suggest a role for geographic, ethnic and dietary factors in the etiology of colorectal MA. For rectal cancer, the incidence of MA was 3 times greater among men than among women, whereas it was two times higher for NMA. This preponderance of MA in men with rectal cancer ($p<0.01$) agrees with other research (4,15,17). Our finding of no gender or age difference between MA and NMA incidence for colon and rectal cancers combined ($p=0.09$ and 0.30, respectively) is similar to other study results (9,31).

Our results did not support the findings that MA of the colon and rectum presented at a later stage than did NMA (17,18,32). Instead, our data showed that MAs and NMAs were most frequently diagnosed at stages II and III, followed by stages IV and I. No significant differences in stage were found between MA and NMA, both by site and overall, when similar findings have been reported only for overall colorectal cancer (9,13).

The ORCC cancer reporting system is based on pathology and cytology reports, clinical records and death certificates. This multiple reporting practice provides an accurate and complete set of data for each patient. All the cancer cases in this study were histologically confirmed. Patients' survival status was obtained through active and passive follow-up, including record linkage with the Ontario Mortality Database. The proportion of patients lost to follow-up was 0.8% for the overall cohort. While incomplete case ascertainment may influence external comparisons to other populations, it is unlikely to have affected comparisons made between the MA and NMA cohorts.

It remains in doubt whether or not MA adversely affects survival. Disparity in the criteria for defining MA and NMA, case selection, sample size of the MA population, duration of follow-up and statistical adjustments may explain some of the contradictions concerning the prognosis of MA patients. For example, studies that included signet ring cell carcinoma in the MA group (31) or excluded poorly-differentiated carcinoma from the NMA group (10,11,33) would increase the difference in survival between MA and NMA patients, given the fact that signet ring cell carcinoma or poorly-differentiated diseases are associated with a particularly worse prognosis compared with their counterparts. These exclusions may have biased the results. Another example is variability in the percentage of mucinous component in the diagnosis of MA. The required amount varied from 50 to >80% in the different series (3,7,15,19).

In conclusion, no statistically significant differences in stage distribution and overall survival were found between MA and NMA patients for colon, rectum and their combination. However, when the stages were considered separately, patients with MA had worse survival than patients with NMA for stage III diseases of both sites. Grading differentiation contributed useful discriminatory information concerning this prognosis difference within stage III. Multivariate analysis of combined data for colon and rectal cancers showed that independent and significant prognostic factors were stage for MA, with age and grade as well as stage for NMA. Disparity in the criteria for defining MA and NMA as well as case selection may explain some of the contradictions on the prognosis of MA in the literature.

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