Br. J. Surg. 1985, Vol. 72, September, 715–718

Peculiarities of mucinous colorectal carcinoma

H. C. Umpleby, D. L. Ranson and R. C. N. Williamson

University Department of Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, UK

Correspondence to: Professor R. C. N. Williamson

The clinical and pathological features of 54 mucinous carcinomas of the large intestine were compared with those of 576 non-mucinous carcinomas. Tumours were only categorized as mucinous if they contained at least 60 per cent of mucin by volume. Those with a moderate mucin content (60–80 per cent) were indistinguishable in behaviour from 'non-mucinous' tumours. By contrast, those with a high mucin content (>80 per cent) showed several differences from non-mucinous cancers: they had a more proximal distribution through the large intestine, they comprised a greater fraction of cancers in the under 50 age group (24 versus *7 per cent: P<0·01), they were more likely to be Dukes' stage 'D' (58* versus *31 per cent: P<0·01) and local fixity was commoner (70* versus *37 per cent: P<0·001). Consequently the overall resection rate was reduced from 90 to 73 per cent (P<0·01), the curative resection rate from 69 to 42 per cent (P<0·01) and the 5-year survival rate from 37 to 18 per cent (P<0·05). Colorectal carcinomas of high mucin content require wide excision, tend to recur locally and carry a poor prognosis.*

Keywords: Colorectal carcinoma, mucinous carcinoma

Mucinous carcinoma of the large bowel is a histological variant present in 10–20 per cent of all patients with colorectal cancer[1–4]. The clinical relevance of this particular type of tumour is uncertain. Some reports show a reduction in 5-year survival of up to 20 per cent when compared with non-mucinous tumours[2,5,6], whereas another describes equivalent survival rates[1]. The possibility arises that mucinous carcinomas are not a homogeneous group and that their behaviour could reflect the amount of mucin they contain.

We have compared the clinicopathological features of 54 colorectal carcinomas containing at least 60 per cent of mucin by volume with those of 576 non-mucinous carcinomas.

Patients and methods

Detailed histological reports were available for 669 of 744 patients with carcinoma of the large bowel (90 per cent), who presented to the surgical departments of the Bristol Royal Infirmary between 1 January 1969 and 31 December 1975. Ninety-three patients (14 per cent) were reported to have mucinous carcinomas and 576 had non-mucinous carcinomas. To assess the accuracy of the original histopathology reports and to avoid observer variation[7], available sections from 67 mucinous tumours were compared with those from 75 non-mucinous tumours selected at random. Sections were reviewed by a single pathologist (D.L.R.) without reference to the original reports.

According to the criteria described by Symonds and Vickery[2], a carcinoma was only described as 'mucinous' if at least 60 per cent of the tumour's volume consisted of mucin. Tumours in which surface mucin only was present were specifically excluded. Of the 67 so-called mucinous sections reviewed, only 54 (81 per cent) fulfilled these criteria. In most of the other 13 mucin was confined to the surface of the tumour. The true mucinous lesions included 33 in which mucin composed more than 80 per cent of tumour volume ('high mucin content') and 21 in which mucin comprised 60–80 per cent of tumour volume ('moderate mucin content'). Not one of the 75 non-mucinous sections reviewed was reclassified as mucinous.

In 51 of 54 mucinous carcinomas the degree of histological differentiation was reassessed; the material was inadequate in the other 3 cases. Histological grading of mucinous tumours is controversial, since the production of mucin might be taken to indicate a physiological function, i.e. a differentiated tumour. However, lesions were graded on morphological grounds only. Information was available from the original histopathology reports in 569 non-mucinous carcinomas, and this grading was confirmed in the 75 lesions checked.

The clinical and pathological features of the 54 true mucinous carcinomas were compared with those of the 576 non-mucinous carcinomas, with particular regard to patterns of recurrence and eventual outcome. The 13 reclassified tumours and the 26 mucinous lesions unavailable for review have been excluded from further analysis. Complete 5-year follow-up was obtained for all patients with mucinous carcinoma and 556 of 576 patients with non-mucinous carcinoma. The χ^2 test with Yates' correction for continuity was used to compare the significance of differences in distribution.

Results

Incidence

To calculate the relative proportions of the mucinous and non-mucinous variants of adenocarcinoma, we have made two assumptions. Firstly, since none of the 75 non-mucinous cancers that we sampled needed reclassification, the absence of a 'mucinous' label in the original report has been taken to exclude that type. Secondly, the proportion of true mucinous lesions might reasonably be the same among those unavailable for histological review ($n=26$) as it was among those reviewed ($n=67$). Granted these assumptions, we find that true mucinous carcinomas represent 11 per cent of all carcinomas of the large intestine (75 of 669).

There were 25 males and 29 females with mucinous carcinoma, 288 males and 288 females with non-mucinous carcinoma. The mucinous pattern was particularly prevalent among younger patients (*Table 1*). Thus 19 per cent of patients under the age of 50 years had mucinous tumours, as opposed to 8 per cent of those over the age of 50 years ($P<0·01$). Likewise 19 per cent of mucinous tumours and 7 per cent of non-mucinous tumours occurred in patients under 50 years of age ($P<0·01$). This age disproportion applied exclusively to tumours with a high (>80 per cent) mucin content, which comprised eight of ten mucinous tumours found among patients aged 50 years or less. Tumours of moderate mucin content showed no such predilection for the young.

Pathology

Site. Nineteen per cent of all mucinous tumours arose in the right colon (caecum and ascending colon), 17 per cent in the

Table 1 *Age distribution of patients with mucinous and non-mucinous adenocarcinomas of the large bowel*

Age group (years)	Mucinous	*P*	Non-mucinous
<50	10	<0·01	42
50–69	24	n.s.	286
>70	20	n.s.	248
Total	54	—	576

0007–1323/85/090715–04$3.00

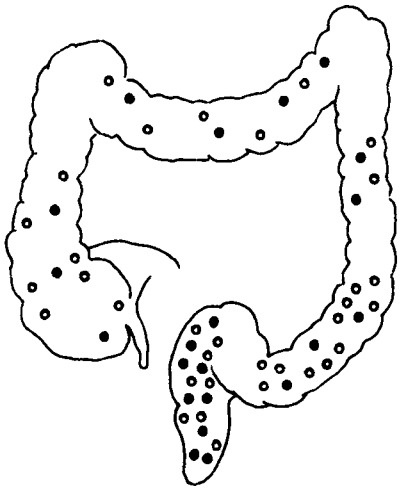

Figure 1 *Distribution of 54 mucinous carcinomas of the large bowel. ●, 60–80 per cent of tumour volume consists of mucin; ○, ⩾80 per cent of tumour volume consists of mucin*

Table 2 *Tumour staging of mucinous and non-mucinous adenocarcinomas of the large bowel*

	Mucinous					
	High mucin content		Moderate mucin content		Non-mucinous	
Dukes' stage	No.	%	No.	%	No.	%
A	—	—	1	5	41	7
B	5	15 *	9	43	198	35
C	9	27	8	38	157	27
'D'	19	58**	3	14	180	31
Total	33	100	21	100	576	100

For multiple carcinomas only the most advanced lesion is included
Significance: * $P<0.05$ *versus* tumours of moderate mucin content, $P<0.01$ *versus* non-mucinous tumours; ** $P<0.01$ *versus* tumours of moderate mucin content, $P<0.001$ *versus* non-mucinous tumours

transverse colon (including the flexures), 33 per cent in the left colon (descending and sigmoid) and 31 per cent in the rectum (including the rectosigmoid) (*Figure 1*). Compared with non-mucinous tumours, a higher proportion of mucinous tumours arose proximal to the splenic flexure (36 *versus* 24 per cent; n.s.), and a lower proportion arose in the rectum (31 *versus* 46 per cent; $P<0.05$). Tumours of high mucin content tended to be commoner than those of moderate mucin content in the right colon (21 *versus* 14 per cent) and less common in the rectum (24 *versus* 43 per cent) but differences did not reach statistical significance.

Stage (*Table 2*). Tumours were staged according to Turnbull's modification of the Dukes' classification[8,9], which includes stage 'D' for incurable disease (local irresectability, distant metastasis) plus (in this study) those dying before operation (8 non-mucinous). Compared with non-mucinous tumours, rather more mucinous tumours were stage 'D' (41 *versus* 31 per cent; n.s.) and fewer were stage A or B (28 *versus* 42 per cent; $P<0.05$). Moreover, lesions of high mucin content were less likely to be Dukes' A and B (15 per cent) than tumours of either moderate mucin content (48 per cent; $P<0.05$) or low mucin content (42 per cent; $P<0.01$). The corollary held true for stage 'D' disease, which was encountered in no less than 58 per cent of lesions with a high content of mucin.

Fixity. Clinical notes were sufficiently detailed to determine tumour fixity for all 54 mucinous carcinomas and for 549 non-mucinous carcinomas. Thirty-five mucinous tumours (65 per cent) were locally fixed compared with 204 (37 per cent) non-mucinous tumours ($P<0.001$). Once again tumour fixity tended to be commoner in high-mucin than moderate-mucin tumours (70 per cent *versus* 57 per cent; n.s.).

Grade (*Table 3*). There were no great differences between the overall proportions of mucinous and non-mucinous cancers in any histological grade; most tumours of each type were moderately differentiated. However, there was a tendency for tumours of high mucin content to be poorly differentiated. There was no consistent relationship between clinical staging and histological grading for tumours of any particular mucin content.

Multiplicity. Four patients with mucinous tumours (7 per cent) had multiple colorectal carcinomas. Two patients developed synchronous mucinous and non-mucinous cancers. One of these and two others developed metachronous carcinomas. Fifteen non-mucinous cancers were multiple (3 per cent), twelve synchronous and three metachronous. In 45 mucinous and 471 non-mucinous cases there were sufficient pathological data to determine the presence or absence of associated adenomatous polyps. Nine mucinous (20 per cent) and 108 non-mucinous (23 per cent) carcinomas were associated with adenomas. Two mucinous carcinomas (4 per cent) were clearly associated with pre-existing villous adenomas, compared with ten non-mucinous carcinomas (2 per cent).

Associated conditions. Total ulcerative colitis was present in one patient who presented with a mucinous carcinoma. Eight of the patients with non-mucinous tumours gave a history of ulcerative colitis, and there was one case of polyposis coli.

Presentation and management

Symptoms and signs. These were the same for mucinous carcinoma as for 'ordinary' large bowel cancer, namely alteration of bowel habit (74 per cent), abdominal pain (69 per cent), subjective weight loss (57 per cent) and rectal bleeding (39 per cent). Fifteen patients (28 per cent) had a palpable mass on rectal examination, including eleven of the seventeen patients with a rectal tumour. Twenty-three patients (43 per cent) had an abdominal mass, including eight of the ten patients with right colon tumours. In 76 per cent of patients the history was less than 6 months in duration and in 57 per cent less than 3 months. Only 8 per cent of patients gave a history of more than 1 year. Symptom duration was similar in patients with non-mucinous cancers.

Emergency admission. The incidence was similar for mucinous and non-mucinous tumours (24 per cent and 30 per cent). Intestinal obstruction was the commonest cause of emergency admission, occurring in 17–19 per cent of cases irrespective of histological type.

Resectability. One elderly patient with a disseminated mucinous carcinoma and 12 patients with non-mucinous

Table 3 *Histological differentiation of mucinous and non-mucinous adenocarcinomas of the large bowel*

	Mucinous					
	High mucin content		Moderate mucin content		Non-mucinous	
Dukes' stage	No.	%	No.	%	No.	%
Good	6	19	6	30	145	27
Moderate	17	55	13	65	336	59
Poor	8	26	1	5	88	15
Total	31	100	20	100	569	100

For multiple carcinomas only the least differentiated lesion is included

carcinoma did not come to laparotomy. Both the overall resectability and the curative resection rate were lower for tumours of high mucin content than for those of moderate mucin content or non-mucinous tumours (*Table 4*). Local spread prevented a curative resection in 12 of the 21 mucinous cancers found to be incurable at operation, whereas disseminated disease was more often the reason in non-mucinous cancers. Moreover, resection of contiguous organs (uterus, ovary, bladder, small bowel, stomach, abdominal wall) was more often required for mucinous than non-mucinous lesions, though neither of these differences quite reached statistical significance.

Curative resection rates in mucinous carcinoma were independent of age, sex and anatomical site. They were affected by the degree of histological differentiation, being 75 per cent for well-differentiated, 60 per cent for moderately differentiated and 44 per cent for poorly differentiated tumours; tumour differentiation had a similar influence in non-mucinous carcinomas. Elective mucinous cases were much more likely than emergency cases to undergo curative resection (71 per cent *versus* 17 per cent; $P<0.01$).

Postoperative mortality. There were seven postoperative deaths in patients with mucinous tumours (13 per cent). Three patients developed generalized faecal peritonitis, from anastomotic dehiscence, necrotizing enterocolitis and small bowel infarction secondary to a superior mesenteric artery embolus. Four patients died from bronchopneumonia. The postoperative mortality rate in patients with non-mucinous tumours was similar (16 per cent).

Outcome

Recurrence. Following curative resection of a mucinous carcinoma 5 patients died in the postoperative period, leaving 27 patients for potential recurrence. Nineteen of these actually developed recurrent disease (70 per cent); by contrast 136 of 293 available patients with non-mucinous tumours (46 per cent) developed recurrence ($P<0.05$). Recurrence was particularly likely in cancers of high mucin content (79 per cent). Similar numbers of mucinous and non-mucinous tumours recurred within 2 years (58 per cent *versus* 66 per cent), but no less than 21 per cent of recurrent mucinous tumours were detected beyond 5 years, as opposed to 4 per cent of recurrent non-mucinous tumours ($P<0.02$). Local recurrence accounted for 37–50 per cent of cases and was not significantly affected by the mucin content of the original lesion.

Survival. Corrected survival rates were employed to distinguish between cancer and non-cancer related deaths. Excluded from analysis were patients dying in the postoperative period after apparently complete resection of tumour (mucinous 5, non-mucinous 52), those dying within 5 years of operation without clinical or postmortem evidence of recurrent disease (non-mucinous 42) and those with incomplete 5 year follow-up (non-mucinous 10). Only 12 of the total 54 patients with mucinous carcinoma were alive 5 years after diagnosis, giving a crude (uncorrected) 5-year survival rate of 22 per cent. Corrected 5-year survival rates were lower for mucinous than non-mucinous tumours both overall (24 per cent *versus* 37 per cent; n.s.) and after potentially curative resection (44 per cent *versus* 57 per cent; n.s.) (*Figure 2*). However, carcinomas of high mucin content had a reduced overall survival compared to those of moderate mucin content (18 per cent *versus* 37 per cent; $P<0.05$).

Younger patients (< 50 years old) with mucinous carcinoma fared particularly badly, with a corrected 5-year survival rate of 20 per cent compared with 50 per cent in non-mucinous cases. Tumour stage influenced overall survival largely irrespective of histological type (*Table 5*). The single patient with a mucinous Dukes' A lesion died postoperatively. There was a tendency for Dukes' B lesions of high mucin content to do badly, whereas Dukes' C lesions had a reasonable prognosis. Histological differentiation also affected survival. Mucinous and non-mucinous tumours of good or moderate differentiation had similar overall 5-year survival rates (30–45 per cent), whereas poorly differentiated tumours had reduced survival (0–17 per cent; $P<0.001$).

Table 4 *Operability and resectability of mucinous and non-mucinous adenocarcinomas of the large bowel*

	Mucinous					
	High mucin content		Moderate mucin content		Non-mucinous	
	No.	%	No.	%	No.	%
All cases	33	100	21	100	576	100
Operation	32	97	21	100	562	98
Resection	24	73*	21	100	517	90
'Curative resection'	14	42**	18	86	397	69
Resection incl. contiguous organs	7	21	5	24	73	13
Incurable at operation	18	56**	3	14	159	28
Dissemination	9	27	0	0	107	19
Local spread	9	27	3	14	52	9

Significance: *$P<0.05$ *versus* tumours of moderate mucin content, $P<0.01$ *versus* non-mucinous tumours; **$P<0.01$ *versus* tumours of moderate mucin content and *versus* non-mucinous tumours

Discussion

Estimating the true incidence of mucinous carcinoma has been hampered by the lack of a uniformly accepted definition for this type of large bowel cancer. Some degree of mucin production is characteristic of all colorectal carcinomas, but the term 'mucinous' has generally been restricted to tumours in which mucin predominates[1,4]. Further confusion can arise from the use of the term 'colloid carcinoma' to describe those lesions with a gelatinous appearance of the cut surface. The quantitative criteria of Symonds and Vickery[2] provide an objective definition of the mucinous tumour. Our overall incidence of 11 per cent (in the UK) corresponds to figures of 15 per cent in the USA[2] and 13·5 per cent in Argentina, another country with a high prevalence of large bowel cancer[4]. A greater proportion of

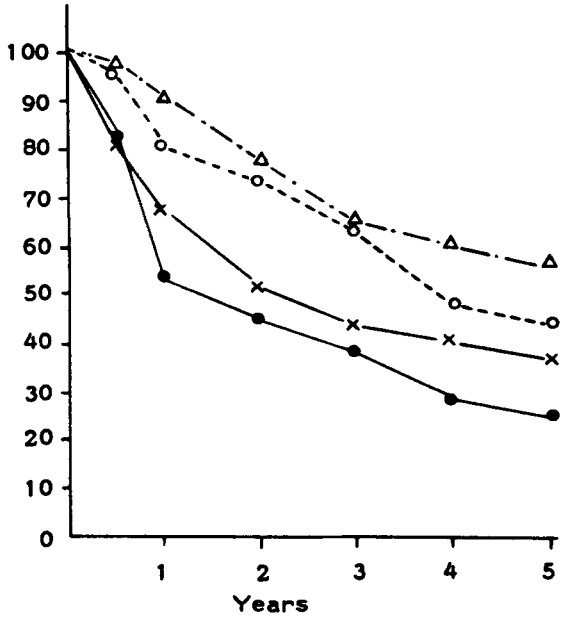

Figure 2 *Corrected survival rates for mucinous and non-mucinous carcinomas of the large bowel: all cases and those requiring curative resection.* ×, *overall non-mucinous* (n = *472*); ●, *overall mucinous* (n = *49*); △, *curative non-mucinous* (n = *302*); ○, *curative mucinous* (n = *27*)

Table 5 *Survival according to tumour stage in patients with mucinous and non-mucinous carcinoma of the large bowel*

	High mucin content			Moderate mucin content			Non-mucinous		
		Survival 5 years			Survival 5 years			Survival 5 years	
	No. of patients	No.	%	No. of patients	No.	%	No. of patients	No.	%
A	—			—			25	24	96
B	5	2	40	5	3	60	147	110	75
C	9	4	44	8	3	38	120	38	32
'D'	19	0	0	3	0	0	180	3*	2
Total	33	6	18	16	6	38	472	175	37

Figures exclude postoperative deaths after potentially curative resection and deaths within 5 years without clinical or post-mortem evidence of recurrent disease. *Liver metastases suspected at operation but no biopsy taken

mucinous carcinomas (26–31 per cent) is reported in countries with a low overall prevalence of large bowel cancer, e.g. Zaire and Jordan[10,11]. This discrepancy could reflect the greater number of young patients with colorectal cancer among low-risk populations[10]. In support, studies of high-risk populations have shown mucinous carcinoma in up to 40 per cent of patients under the age of 40 years[12–14]. The present series confirms this unequal distribution: 19 per cent of patients below 50 years have mucinous cancer. The increased incidence of mucinous tumours in the young is sometimes thought to account for their poor prognosis[11–14]. In Bristol, however, young patients (40 years and below) with large bowel cancer fared no worse than their seniors, any increased tendency to a more virulent type of neoplasia being balanced by a greater tolerance of emergency resection[15].

Our data shed some light on the most controversial aspect of mucinous adenocarcinomas of the large intestine, namely whether or not they have a less favourable outcome than ordinary cancers. We find that clinical behaviour closely parallels the percentage content of mucin. Cancers of moderate mucin content (60–80 per cent by volume) are indistinguishable from 'non-mucinous' cancers (< 60 per cent): they have the same age and anatomical distribution, the same spectrum of clinical stage and histological grade, the same resectability rates and 5-year survival. By contrast, cancers of high mucin content (> 80 per cent) affect a younger age group, arise in proximal colon rather than rectum, are 2–4 times as likely to be incurable at presentation (generally owing to local invasion and fixity) and are often poorly differentiated. As a consequence of these unfavourable characteristics, their overall resection rate, curative resection rate and 5-year survival rate are significantly poorer. Four in five recur, and recurrence can be seen even after 5 years.

Early and extensive invasion is an established feature of mucin-secreting tumours in both man[1,2] and experimental animals[16]. Perhaps the tenacious mucus overcomes tissue resistance and facilitates local spread[1]. This tendency to local invasion explains the frequency with which mucinous tumours are found adherent to adjacent structures at laparotomy. Thus contiguous organs may need to be excised and there is impaired survival in Dukes' B lesions. Contrariwise, Dukes' C mucinous lesions in our series had marginally better survival rates than their non-mucinous counterparts, conceivably because mucin secretion limits dissemination beyond the regional lymph nodes[1].

These findings have two practical consequences. Firstly, if pre-operative biopsy of a colorectal cancer shows a high mucin content, the surgeon should expect to encounter a tumour that is locally advanced and may require wide excision including adjacent viscera. Secondly, the high risk of recurrent carcinoma dictates thorough postoperative surveillance, which must be extended beyond 5 years. Since recurrence is local in up to half the cases, some patients might merit a 'second-look' laparotomy. Lastly redefining mucinous carcinomas as those containing at least 80 per cent of mucin by volume should identify a distinct subset of cancers that carry a particularly poor prognosis.

Acknowledgements

We are grateful to the surgeons of the Bristol Royal Infirmary for allowing us to study their patients. Mr Umpleby was a Wellcome Research Fellow, and we are indebted to the Wellcome Trust for their financial support.

References

1. Wolfmann EF, Astler VB, Coller FA. Mucoid adenocarcinoma of the colon and rectum. *Surgery* 1957; **42**: 847–52.
2. Symonds DA, Vickery AL. Mucinous carcinoma of the colon and rectum. *Cancer* 1976; **37**: 1891–1900.
3. Hoth DF, Petrucci PE. Natural history and staging of colon cancer. *Semin Oncol* 1976; **3**: 331–6.
4. Sundblad AS, Paz RA. Mucinous carcinoma and polyps. *Cancer* 1982; **50**: 2504–9.
5. Trimpi HD, Bacon HE. Mucoid carcinoma of the rectum. *Cancer* 1951; **4**: 597–609.
6. Grinnell RS. The grading and prognosis of carcinoma of the colon and rectum. *Ann Surg* 1939; **109**: 500–33.
7. Blenkinsopp WK, Stewart-Brown S, Blesovsky L, Kearney G, Fielding LP. Histology reporting in large bowel cancer. *J Clin Pathol* 1981; **34**: 509–13.
8. Turnbull RB Jr, Kyle K, Watson FR, Spratt I. Cancer of the colon: the influence of the *no-touch isolation* technic on survival rates. *Ann Surg* 1967; **166**: 420–27.
9. Dukes CE. The classification of cancer of the rectum. *J Pathol* 1932; **35**: 323–32.
10. Ngala Kenda JF. Cancer of the large bowel in Africa. A 15-year survey at Kinshasa University Hospital, Zaire. *Br J Surg* 1976; **63**: 966–8.
11. Dajani YF, Zayed I, Malatjabian DA, Kamal MF. Colorectal cancer in Jordan and Nova Scotia. A comparative epidemiologic and histopathologic study. *Cancer* 1978; **46**: 420–6.
12. Recalde M, Holyoke ED, Elias EG. Carcinoma of the colon, rectum and anal canal in young patients. *Surg Gynecol Obstet* 1974; **139**: 909–13.
13. Hall A, Coffey RJ. Cancer of the large bowel in the young adult. *Am J Surg* 1961; **102**: 66–72.
14. Chappell FW. Carcinoma of the colon in young people. *Am Surg* 1959; **25**: 449.
15. Umpleby HC, Williamson RCN. Carcinoma of the large bowel in the first four decades. *Br J Surg* 1984; **71**: 272–7.
16. Williamson RCN, Davies PW, Bristol JB, Wells M. Intestinal adaptation and experimental carcinogenesis after partial colectomy: increased tumour yields are confined to the anastomosis. *Gut* 1982; **23**: 316–25.

Paper accepted 16 April 1985