British Journal of Surgery 1998, **85**, 355–358

Risk factors for anastomotic leakage after resection of rectal cancer

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Background The most important surgical complication following rectal resection with anastomosis is symptomatic anastomotic leakage, which is associated with a 6–22 per cent mortality rate. The aim of this retrospective study was to evaluate the risk factors for clinical anastomotic leakage after anterior resection for cancer of the rectum.

Methods From 1980 to 1995, 272 consecutive anterior resections for rectal cancer were performed by the same surgical team; 131 anastomoses were situated 5 cm or less from the anal verge. The associations between clinical anastomotic leakage and 19 patient-, tumour-, surgical- and treatment-related variables were studied by univariate and multivariate analysis.

Results The rate of clinical anastomotic leakage was 12 per cent (32 of 272). Multivariate analysis of the overall population showed that only male sex and level of anastomosis were independent factors for development of anastomotic leakage. The risk of leakage was 6·5 times higher for anastomoses situated less than 5 cm from the anal verge than for those situated above 5 cm; it was 2·7 times higher for men than for women. In a second analysis of low anastomoses (5 cm or less from the anal verge; $n = 131$), obesity was statistically associated with leakage.

Conclusion A protective stoma is suitable after sphincter-saving resection for rectal cancer for anastomoses situated at or less than 5 cm from the anal verge, particularly for men and obese patients.

The most important surgical complication following rectal resection with intestinal anastomosis is symptomatic anastomotic leakage. The clinical leakage rate after anterior resection varies from 3 to 19 per cent[1–15], and the mortality rate and risk of permanent stoma after clinical leakage are 6–22 per cent[1,4,7,8,10,12–14,16] and 10–100 per cent[7,8,10,12,13] respectively.

The aim of this retrospective study was to evaluate the risk factors for clinical anastomotic leakage in patients who had rectal resection for cancer.

Patients and methods

Patients

Consecutive patients who underwent rectal resection for cancer with a colorectal or coloanal anastomosis between 1 January 1980 and 31 December 1995 were included in the study. Patients having repeated resection for local recurrence of rectal cancer and colorectal anastomosis after Hartmann's procedure were excluded.

Surgical procedure

All patients were operated on by the same surgical team, more than half (56 per cent) by the senior author (M.P.). The day before operation, bowel lavage with 3 litres of polyethylene glycol was carried out, and all patients received antibiotic prophylaxis for a minimum of 2 days. A midline abdominal incision was performed. The inferior mesenteric artery was ligated at its origin flush with the aorta or just below the ascending left colic artery. The left colon and splenic flexure were mobilized in the majority of low anterior resections to achieve anastomosis without tension. The sigmoid or descending colon was transected. Rectal dissection was carried out 5 cm below the lower edge of tumours in the upper third of the rectum, and to the pelvic floor for mid and low rectal tumours[17]. Rectal irrigation was performed during operation, before transection of the rectum, using povidone–iodine solution for most patients. When the tumour was very low, partial resection of the anal canal was performed by the abdominal approach, or by the perineal approach after everting the anal canal. Minimal distal clearance of the tumour on the fresh specimen was 2 cm.

Anastomoses were hand-sewn or stapled (EEA; CEEA; US Surgical, Norwalk, Connecticut, USA). The doughnuts were always inspected for completeness. Anastomotic integrity was tested during operation by transanal instillation of fluid only for low anastomoses, particularly if there were difficulties in performing the anastomosis or if the doughnuts were incomplete. A colonic J pouch was sometimes used. A protective colostomy or ileostomy was used if there was anastomotic tension, poor bowel preparation, incomplete doughnuts or leakage on testing, or technical difficulties in performing low rectal anastomosis because of the anatomy of the patient, and for all coloanal anastomoses. Pelvic drains, placed behind the anastomosis in the presacral space, were always used.

Some patients who had a tumour with a high risk of local recurrence received preoperative and sometimes intraoperative radiotherapy.

Definition of anastomotic leakage

The definition of anastomotic leakage in the present study was clinical: gas, pus or faecal discharge from the drain, pelvic abscess, peritonitis, discharge of pus per rectum or rectovaginal fistula. All anastomotic leakages were confirmed by water-soluble contrast enema, performed by the surgeon. Extra-anastomotic complications (leak at the apex of the efferent limb of the J pouch, two cases; pelvic abscess without leakage, one case) were not considered as clinical anastomotic leakage. Asymptomatic radiological anastomotic leakages were not considered because routine contrast enema was not performed after operation. Patients who died from general postoperative complications ($n = 5$) before the mean date of clinical anastomotic leakage were considered as unevaluable, and were excluded from the study.

Statistical analysis

A first analysis was carried out on the overall population of patients who had colorectal or coloanal anastomoses. A second

Paper accepted 21 July 1997

analysis was performed only on patients with anastomoses 5 cm or less from the anal verge.

Sixteen independent variables were analysed: age, sex, obesity (20 per cent heavier than ideal body-weight), tumour height (distance between tumour caudal edge and the anal verge), tumour stage (tumour node metastasis (TNM) classification[18]), level of ligation of the inferior mesenteric artery, type of colon used for anastomosis, level of anastomosis from the anal verge,

Table 1 Anastomotic leakage after resection of rectal cancer – univariate analysis

	Overall population ($n = 272$)		Low anastomoses ($n = 131$)	
	No. of patients	*P*	No. of patients	*P*
Sex				
M	25 of 165 (15)	0·03	18 of 75 (24)	0·09
F	7 of 107 (7)		7 of 56 (12)	
Obesity*				
Yes	9 of 54 (17)	0·16	9 of 27 (33)	0·03
No	20 of 204 (10)		15 of 99 (15)	
Tumour height (cm)				
12·5–18	2 of 54 (4)	0·11	—	
6·5–12	22 of 166 (13)		17 of 80 (21)	0·43
3–6	8 of 52 (15)		8 of 51 (16)	
Tumour stage				
T_{1-2}	8 of 80 (10)	0·56	6 of 43 (14)	0·30
T_{3-4}	24 of 192 (12)		19 of 88 (22)	
Inferior mesenteric artery				
High ligation	8 of 66 (12)	0·92	6 of 38 (16)	0·54
Low ligation	24 of 206 (12)		19 of 93 (20)	
Colonic section level*				
Sigmoid	21 of 163 (13)	0·37	16 of 82 (20)	0·69
Descending	10 of 107 (9)		8 of 48 (17)	
Level of anastomosis (cm)				
8·5–15	0 of 44 (0)	0·002	—	
5·5–8	7 of 97 (7)		—	
3·5–5	16 of 84 (19)		16 of 84 (19)	0·99
1·0–3	9 of 47 (19)		9 of 47 (19)	
Type of anastomosis				
Hand-sewn	10 of 121 (8)	0·11	6 of 44 (14)	0·26
Stapled	22 of 151 (15)		19 of 87 (22)	
Configuration of anastomosis				
End to end	23 of 152 (15)	0·08	18 of 86 (21)	0·42
Side to end	8 of 110 (7)		6 of 41 (15)	
End to side	0 of 10 (0)		0 of 4 (0)	
Protective stoma				
Yes	20 of 114 (18)	0·01	16 of 86 (19)	0·85
No	12 of 158 (8)		9 of 45 (20)	
Preoperative radiotherapy				
Yes	4 of 28 (14)	0·66	4 of 25 (16)	0·66
No	28 of 244 (11)		21 of 106 (20)	
Intraoperative radiotherapy				
Yes	4 of 19 (21)	0·19	4 of 17 (24)	0·62
No	28 of 253 (11)		21 of 114 (18)	
Quality of resection				
Curative	29 of 239 (12)	0·61	23 of 121 (19)	0·94
Palliative	3 of 33 (9)		2 of 10 (20)	
Length of intervention (h)				
≤ 4	11 of 148 (7)	0·01	8 of 46 (17)	0·72
> 4	21 of 124 (17)		17 of 85 (20)	
Operator				
Colorectal surgeon	29 of 204 (14)	0·03	24 of 113 (21)	0·12
Digestive surgeon	3 of 68 (4)		1 of 18 (6)	
Colonic pouch				
Yes	—		3 of 19 (16)	0·77
No	—		22 of 112 (20)	
Anal canal resection				
Yes	—		4 of 22 (18)	0·90
No	—		21 of 109 (19)	
Anal canal eversion				
Yes	—		2 of 10 (20)	0·95
No	—		23 of 121 (19)	

Values in parentheses are percentages. *Clinical data not complete for all patients. Age was not associated with leakage for the overall population ($P = 0·95$) or for those with low anastomoses ($P = 0·60$)

Table 2 Features of clinical anastomotic leakage after resection of rectal cancer

	No. of patients
Gas, pus or faecal discharge from drain	21
Pelvic abscess	3
Peritonitis	2
Discharge of pus per rectum	2
Rectovaginal fistula	4
Total	32

type of anastomosis (stapled or sutured), configuration of anastomosis (end to end, end to side or side to end), protective stoma, preoperative radiotherapy, intraoperative radiotherapy, quality of resection (curative *versus* palliative), length of intervention, and operator (colorectal *versus* digestive surgeons). For the second analysis, three other variables were included: colonic pouch, anal canal resection and anal canal eversion.

The association of leakage and independent variables was studied by univariate analysis (χ^2 test, Student's t test and Fisher's exact test for small groups). All variables associated with leakage with $P \leq 0{\cdot}2$ were considered for multivariate analysis. Multiple logistic regression was first done on this full model. Variables were eliminated one at a time, beginning with the variable having the highest P value. $P \leq 0{\cdot}05$ was considered significant.

Results

Patients

The first analysis included 272 patients with rectal resection. There were 165 men and 107 women (sex ratio 1·5) with a mean(s.d.) age of 64(12) (range 25–91) years. Some 239 procedures (88 per cent) were curative and 33 (12 per cent) were palliative.

The second analysis concerned 131 patients with low anastomoses: 75 men and 56 women (sex ratio 1·3) of mean(s.d.) age 63(11) (range 25–83) years. Details of the clinical characteristics of the two groups are shown in *Table 1*.

Anastomotic leakage

The rate of clinical anastomotic leakage was 12 per cent (32 of 272) in the overall population of patients having rectal resection, and 19 per cent (25 of 131) in the group with low anastomoses. No patient with anastomosis more than 8 cm from the anal verge had leakage. The mean postoperative period of diagnosis for clinical leakage was 11 (range 2–41) days. The different types of clinical anastomotic leakage are presented in *Table 2*; the majority were minor leakages.

In the first study (all anastomoses; $n = 272$), univariate analysis showed five variables to be associated with the risk of anastomotic leakage: sex ($P = 0{\cdot}03$), level of anastomosis ($P = 0{\cdot}002$), stoma ($P = 0{\cdot}01$), length of intervention ($P = 0{\cdot}01$) and operator ($P = 0{\cdot}03$) (*Table 1*). Multivariate analysis showed that only sex and level of anastomosis were independent associated factors for the development of anastomotic leakage. The risk of leakage was 2·7 times higher for men than for women ($P = 0{\cdot}03$; 95 per cent confidence interval (c.i.) 1·07–6·76). It was 6·5 times higher for anastomoses situated at or below 5 cm from the anal verge than for those higher than 5 cm ($P < 0{\cdot}001$; 95 per cent c.i. 2·37–17·87).

In the second analysis (low anastomoses; $n = 131$), obesity was significantly associated with leakage ($P = 0{\cdot}03$), and sex was not far from the level of significance ($P = 0{\cdot}09$) (*Table 1*). The anastomotic leakage rate after low colorectal and coloanal anastomoses was 33 per cent (nine of 27) for obese patients and 15 per cent (15 of 99) for non-obese patients. It was 24 per cent (18 of 75) for men and 12 per cent (seven of 56) for women.

Leakage and reoperation

Of the 32 patients with clinical anastomotic leakage, 13 had a second surgical intervention. The risk of reoperation was two times greater for patients without a stoma than for those with a stoma (seven of 12 *versus* six of 20, $P = 0{\cdot}31$). One patient died after leakage. A 66-year-old man had a coloanal anastomosis for a low Dukes C2 rectal cancer. A protective, but unfortunately not defunctioning, stoma was performed with transverse colon. Peritonitis appeared on day 6 after operation. The anastomosis was removed, and excision of the anal canal and a definitive stoma were carried out. The patient died 23 days after reoperation from myocardial infarction.

Discussion

The relatively high rate of clinical anastomotic leaks of 12 per cent in this series, compared with 3–19 per cent reported in recent studies[1–15], is due to the fact that about half (48 per cent; 131 of 272) of the anastomoses in the present series were very low, situated 5 cm or less from the anal verge, and because sphincter-saving resection for narrow pelvis, obese patients or very low tumours was rarely avoided[19]. However, the postoperative mortality rate after clinical anastomotic leakage was low (one patient), the majority of leakages were minor, and no patient had leakage from an anastomosis situated more than 8 cm from the anal verge.

Colorectal surgeons (M.P. and E.R.) had a higher rate of leakage than other surgeons (J.S. and junior digestive surgeons) because they performed the majority of low colorectal anastomoses and all coloanal anastomoses. Stoma formation and operating time were associated with increased risk of leakage in univariate analysis but were not found to be independent factors of leakage in multivariate analysis, because protective stoma and long operations were often associated with low anastomosis, which was the most important predictive factor for leakage. In the second analysis, performed only with low anastomoses, the leakage rate was the same with or without a stoma (19 *versus* 20 per cent, $P = 0{\cdot}85$) and after a short or a long operation (17 *versus* 20 per cent, $P = 0{\cdot}72$).

Level of anastomosis, male sex and obesity were significantly associated with anastomotic leakage. These results suggest that these patient-related variables are more important than surgeon-related variables for risk of clinical leakage after sphincter-saving resection for rectal cancer.

Most studies that have compared high and low anterior resection have shown that, apart from emergency presentation (obstruction, perforation), the level of anastomosis is the most important predictive factor for leakage[1,2,4,6,10,12–15]. The high-risk level for anastomotic leakage was less than 7 cm from the anal verge for Pakkastie *et al.*[13], less than 6 cm for Karanjia *et al.*[12] and below 5 cm for Heald and Leicester[2].

Analysis of the literature shows that it is difficult to associate some variables with the risk of leakage, because

studies rarely report the results of multivariate analysis. Thus, the contribution of the level of anastomosis, which may confound any other relationship, could not be studied. Moreover, most series reporting an analysis of factors associated with leakage include colonic with rectal resections[1,2,6,8,13,15,16,20]. On the other hand, some multicentre studies have shown that the surgeon could be a risk factor for leakage[1,21]. This is due to specific technical factors that make anastomosis safe: bowel preparation, pelvic haemostasis, colonic blood supply, anastomotic tension, complete doughnuts and intraoperative testing of the anastomosis[22–27]. The present authors therefore believe that the level of anastomosis, the type of patient (sex and obesity) and specific technical difficulties are the major risk factors for anastomotic leakage after rectal resection.

Use of a protective stoma in colorectal anastomoses seems not to decrease the leakage rate[4,5,7,12,13,23], but it does reduce the risk of reoperation and postoperative death if leakage is present[21,23,28]. For this reason, the majority of authors[5,7,12,14,20,21,26,28] recommend creating a protective stoma after anterior resection for patients with a high risk of anastomotic leakage. High anterior resections (anastomosis greater than 8 cm from the anal verge) are considered as colonic resections[1,21]; the leakage rate is low (zero in the present study) and a stoma is not useful. The high-risk population is limited to those undergoing low anterior resection.

Based on this experience, the authors recommend creating a protective stoma after sphincter-saving resection for rectal cancer for all anastomoses situated 5 cm or less from the anal verge, in particular for men and obese patients, with the objective of decreasing the risk of reoperation and the postoperative mortality rate.

Acknowledgements

The authors are grateful to Paul Crocker for reviewing the manuscript.

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