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The Effect of Obstruction and Perforation on Colorectal Cancer Disease-Free Survival

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Abstract
Background Obstruction (OBSTR) and perforation (PERF) in colorectal cancer impact adversely upon outcomes, and cancer-related survival may also be affected. However, data are sparse, particularly on disease-free survival (DFS) where the cancer is both obstructed and perforated (OBS-PERF).
Methods Data were extracted from a prospectively collected database of 1876 colorectal cancer patients managed and followed up at the Royal Brisbane Hospital from 1984 to 2004. The patients who had curative surgery ($n = 1426$) were classified as OBSTR ($n = 153$), PERF ($n = 53$), OBS-PERF ($n = 19$), and uncomplicated (UNCOM; $n = 1201$). Kaplan-Meier survival and Cox proportional hazard analyses were performed.
Results Postoperative mortality within 30 days of surgery was 1.5% ($n = 22$) and the overall complication rate was 40.8% ($n = 582$). However, only 7.2% ($n = 102$) required reoperations. The median survival time was 71 (IQR = 64.9–77.1) months and the median follow-up for DFS was 37.5 (IQR 14–68) months. The overall recurrence rate was 32.7% ($n = 466$), the local recurrence rate was 9.4% ($n = 135$), and local and distant recurrences occurred in the same patient in 4.7% ($n = 67$). Male gender, OBSTR, PERF, OBS-PERF, emergency operation, major medical and surgical complications, reoperation, TNM staging, tumor grading, and tumor venous invasion adversely affected DFS ($p < 0.05$). Multivariate analysis showed that OBS-PERF ($p = 0.008$), major medical complications ($p = 0.011$), reoperation ($p = 0.018$), TNM staging ($p < 0.001$), grading ($p = 0.018$), and venous invasion ($p = 0.002$) were independently associated with a poorer DFS.
Conclusions OBS-PERF colorectal cancer is associated with a poorer DFS, which may be worse than either OBSTR or PERF alone.

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Introduction

Colorectal cancer is the second-most common cancer in incidence among men and women in Australia [1]. It is the second-most common cause of cancer death on that continent and is also a significant health burden to other parts of the world. This disease remains the third most-common cause of death in Western Europe and North America [2]. About one-third of colorectal cancer patients present as an emergency [2], and the emergency situation has been associated with high postoperative mortality rates and poor survival [3–9]. Emergency situations are most commonly related to the complications of tumor obstruction (OBSTR) or tumor perforation (PERF). OBSTR cancers have been reported to have a poor prognosis, with a 5-year survival

probability ranging from 0.12 to 0.31 [3, 10–14]. PERF cancers are relatively uncommon [15, 16] and have been reported to have a poor prognosis [17] and high risk of recurrence [18].

However, in our clinical experience with a cohort of colorectal cancer patients in a specialist colorectal unit, such a grim prognosis for OBSTR and PERF cancers had not necessarily been the case. Most of these patients had also been initially managed at a time when adjuvant therapy was not routinely considered. In addition, there was a small group of patients in which the cancer was both obstructed and had perforated (OBS-PERF) and which appeared to behave differently. A review of the literature had found little data on such OBS-PERF cancers, particularly with regard to eventual cancer recurrences and patient disease-free survival (DFS). Therefore, we decided to analyze our database with regard to the outcomes in patients with OBSTR, PERF, OBS-PERF, and uncomplicated colorectal cancers (UNCOM) who had undergone curative surgery.

Methods

Data from patients presenting with colorectal cancer to the Colorectal Surgical Unit of the Royal Brisbane Hospital between 1984 and 2004 were accessed from a prospectively maintained database. This database contained demographic, clinical, operative, pathologic, and follow-up data. Ethics committee approval from the relevant Hospital Authority and informed consent from patients were obtained. The records showed whether the cancers were UNCOM or complicated by OBSTR, PERF, or OBS-PERF. The classifications of OBSTR, PERF, and OBS-PERF were based on clinical, radiologic, and operative findings, independent of whether the operation was classified as an emergency procedure. The data from patients considered to be cured with no macroscopically detectable residual disease (including cancer-positive resection margins) were reviewed in detail for age; gender; presenting symptom (including obstruction, bleeding, anemia, and urinary symptoms); duration of symptoms prior to consultation; preoperative serum carcinoembryonic antigen (CEA) level ($\leq$5, 6-40, 41-100, >100); preoperative hemoglobin ($\geq$12 g%, <12 g%); preoperative urea (<6.7 mmol/L, $\geq$6.7 mmol/L); preoperative potassium ($\geq$3 mmol/L, hypocalcemia), family history (at least one-first-degree relative with documented colorectal cancer); site of cancer; decade of operation (1984–1993, 1994–2004); operative procedure; elective or emergency nature of surgery; hospital stay; stage, grade, and histopathology of tumor; chemotherapy and radiation therapy provided; and current patient status. Site of cancer was classified as ascending colon, transverse colon, splenic flexure, descending colon, sigmoid colon, or rectum. Primary cancer site in the rectum was further classified according to rigid sigmoidoscopy measurements into the distal rectum (<8 cm), midrectum (8 to <12 cm) and upper rectum 12 to <16 cm). Procedures were classified as "emergency" in the database when performed in the designated emergency operating theatres, outside of the routine "elective" colorectal surgery operating theatre lists. Postoperative complications were noted and classified as medical or surgical complications. Need for reoperations was noted. The tumor node metastasis (TNM) stage was documented and histologic grade assigned according to the World Health Organization criteria (well differentiated, moderately differentiated, or poorly differentiated), as well as the presence or absence of mucin. Exclusion criteria were nonadenocarcinoma histology (i.e., squamous or carcinoid) and familial adenomatous polyposis.

Patients were routinely followed up by a protocol consisting of visits every 3 months for the first 2 years, followed by visits every 6 months for the following 3 years, and annual visits thereafter. CEA levels were reviewed at each visit, and computed tomography of the abdomen, pelvis, and thorax was performed at 2 years follow-up. Colonoscopy was performed 1 year after surgery when the colon and rectum had previously been cleared of synchronous lesions, and repeated at 3-year intervals unless otherwise indicated by findings. Apart from this, patients were investigated in further detail as appropriate to clinical symptoms and findings.

Statistical analysis

Numerical data are given as mean value and standard deviation (SD) or median value and interquartile range (IQR), depending on the distribution. Comparisons between characteristics were conducted using χ^2 tests and χ^2 tests for trend, nonparametric Wilcoxon tests, and t tests or analysis of variance.

Follow-up time is given as median value and interquartile range (IQR). DFS time was calculated as the time between the date of operation and the date of first recurrence or last observation. Cumulative DFS probabilities were calculated using the method of Kaplan-Meier and compared with log-rank tests. Five-year cumulative survival probabilities are presented with 95% confidence intervals (95% CI). Multivariable Cox proportional hazard analysis was conducted for DFS. All variables were dummy-coded in preparation for multivariable analysis. Two-way interactions were considered. After a model was established, all remaining and non-collinear variables were considered one by one as potential confounders. A variable was considered a confounder when the estimate of one characteristic in the model changed by 10% or more.

Table 1 Most common reasons for presenting at clinic

Symptom	No. of patients	Percentage of 1426
Altered bowel habits	769	53.9
Abdominal pain	559	39.2
Bleeding without significant anemia (serum hemoglobin ≥12 g%)	508	35.6
Weight loss	364	25.5
Anemia without clinical overt bleeding (serum hemoglobin <12 g%)	250	17.5
Bleeding causing significant anemia (serum hemoglobin <12 g%)	110	7.7
Urinary symptoms	33	2.3

Results were based on 1426 patients with colorectal cancer who were treated with curative intent between 1984 and 2004

Results of the Cox model are presented as relative risk (RR) of death or recurrence together with 95% CI. Statistical analyses were conducted using SPSS for Windows ver. 17 (SPSS Inc, Chicago, IL). Throughout the analysis $p < 0.05$ was considered statistically significant.

Results

Demographics and clinical presentation

Of all 1876 colorectal cancer patients recorded between 1984 and 2004, 1426 patients [54.2% male; mean age = 67 years (SD = 12.3; range = 19–97 years)] were operated on with curative intent and were included in this analysis. The most common reason for presenting was altered bowel habits (53.9%; Table 1). Fifty-five patients (3.9%) were asymptomatic, with cancer found only at screening colonoscopy. OBSTR was diagnosed in 153 patients (10.7%), PERF in 53 (3.7%; one missing information) and OBS-PERF in 19 patients (1.3%). The median duration of initial symptoms was 1 year (IQR = 4-24) for patients undergoing classified elective surgery and 3 months (IQR = 1–12) for patients undergoing classified emergency surgery ($p < 0.001$). Patients with OBSTR were significantly older ($p = 0.021$), had shorter symptom duration ($p < 0.001$), and were more likely classified as having emergency operations ($p < 0.001$) compared to patients with UNCOM (Table 2).

Tumor location and procedures

The anatomical location of the tumors is given in Table 3, and when the lesions were classified by distance from the anal verge measured at rigid sigmoidoscopy, there were 10.3% distal rectum (<8 cm from anal verge), 4.1% midrectum (9–12 cm from anal verge), 3.9% upper rectum (13–16 cm from anal verge), and 81.6% colon (>17 cm) cancers. Compared to UNCOM, OBSTR were more likely in the splenic flexure ($p < 0.001$) and less likely to be rectal cancers ($p < 0.001$) (Table 2).

The most frequent operations performed were right hemicolectomy (32.2%) and anterior resection (33.7; Table 4). When left-sided cancers were complicated by OBSTR, PERF, or OBS-PERF there was a higher chance of resection without primary anastomosis. Compared to UNCOM, more Hartmann's procedures were performed for (1) descending colon cancers for PERF (66.7 vs. 5.1%; $p = 0.033$); (2) sigmoid colon cancers for OBSTR (34.8 vs. 6.1%; $p < 0.001$), PERF (37.5%; $p = 0.001$), and OBS-PERF (44.4%; $p = 0.002$); and (3) rectal cancers for OBSTR (31.3 vs. 2.0%; $p < 0.001$), PERF (30.0%; $p = 0.002$), and OBS-PERF (50%; $p = 0.048$). None of the OBSTR group had endoscopic self-expanding metallic stenting (SEMS) or preliminary diverting stomas during the period studied.

Outcomes

The median postoperative hospital stay was 10.5 days (IQR = [8, 15]). Postoperative mortality within 30 days of surgery was 1.5% (22 of 1426 patients), and the overall postoperative complication rate was 40.8% (582 of 1426 patients; Tables 3 and 5). The latter consisted of 20.3% (118 of 582) of patients with medical complications, 57.4% (334 of 582) of patients with surgical complications, and 22.3% (130 of 582) of patients with both medical and surgical complications. Reoperations were required in 102 (7.2%; Table 3) patients; these included abscess drainage (1.8%, 26 of 1426), enterolysis (0.8%, 11 of 1426), resuture wound (1.1%, 16 of 1426), hemostasis (1.1%, 15 of 1426), and stoma (2.5%, 35 of 1426).

No differences in complication rates were found between patients with OBSTR and patients with PERF compared with UNCOM. OBS-PERF patients had significantly higher total complication (68.7 vs. 39.9%; $p = 0.017$), major medical complication (42.1 vs. 16.2%; $p = 0.007$), and reoperation (21.1 vs. 6.6%; $p = 0.035$) rates. The major surgical complication rate in this group (10.5 vs. 9.9%) was not significantly different.

Tumor characteristics

Most of the adenocarcinomas (84.8%, 1209 of 1426) were without significant mucinous or signet ring features (Table 3). The majority of cancers were found to be stage II (47.9%, 661 of 1380). Most cancers showed characteristics of moderate differentiation (58.1%, 1142 of 1426), and 38% of cancers were reported to have lymphovascular

Table 2 Characteristics of patients with obstruction (OBSTR) and perforation (PERF) or both (OBS-PERF) in comparison to neither (UNCOM)

	UNCOM ($n = 1200$)	OBSTR ($n = 153$)	PERF ($n = 53$)	OBS-PERF ($n = 19$)
Mean age (SD) (years)	67.3 (12.2)	70.6 (11.8)	63.0 (15.0)	66.1 (15.4)
Overall p value	0.001			
Post-hoc p value*	–	0.021	0.113	0.983
Male (%)	54.7	48.4	62.3	47.4
Overall p value**	0.267			
Median duration of symptoms (IQR) (months)	12 (4, 24)	3 (1, 8)	8 (2, 24.5)	1 (1, 3)
Overall p value	<0.001			
Post-hoc p value*	–	<0.001	0.303	<0.001
Emergency operation (%)	8.2	62.7	39.6	94.7
Overall p value	<0.001			
Post-hoc p value*	–	<0.001	<0.001	<0.001
Site of primary tumour				
Cecum (%)	16.3	11.8	20.8	15.8
Overall p value**	0.392			
Ascending colon (%)	7.9	7.2	1.9	5.3
Overall p value**	0.419			
Hepatic flexure (%)	3.9	7.2	5.7	0
Overall p value**	0.200			
Transverse colon (%)	6.3	11.8	15.1	10.5
Overall p value	0.008			
Post-hoc p value*	–	0.017	0.020	0.340
Splenic flexure (%)	2.7	13.7	1.9	5.3
Overall p value	<0.001			
Post-hoc p value*	–	<0.001	1.0	0.409
Descending colon (%)	3.3	7.8	5.7	5.3
Overall p value	0.029			
Post-hoc p value*	–	0.011	0.418	0.472
Sigmoid colon (%)	21.8	30.1	30.2	47.4
Overall p value	0.005			
Post-hoc p value*	–	0.024	0.174	0.021
Rectum (%)	38.0	10.5	18.9	10.5
Overall p value	<0.001			
Post-hoc p value*	–	<0.001	0.005	0.015

IQR interquartile range

Results were based on 1425 patients with colorectal cancer who were treated with curative intent between 1984 and 2004. One patient record had missing information on perforation

* Post-hoc comparisons versus UNCOM

** No post-hoc comparisons as overall result was not significant

invasion. There were significantly fewer stage I for OBSTR (5.5%, $p < 0.001$) and PERF cancers (5.9%, $p = 0.012$) when compared with UNCOM (22.7%), but this did not reach statistical significance in the OBS-PERF group (0%, $p = 0.070$). No significant differences were found among these groups with respect to the proportion of mucinous cancers ($p = 0.987$), differentiation ($p = 0.188$), lymph node involvement ($p = 0.734$), number of lymph nodes found harvested in the specimen ($p = 0.863$), and venous invasion ($p = 0.114$).

Survival analysis

A total of 58.6% (836 of 1426) of patients died (all causes) and 27.9% (398 of 1424) had a colorectal cancer-related death. The median survival time for all patients was 71 months (IQR = 64.9–77.1). Median follow-up time for DFS was 37.5 months (IQR = 14–68); 32.7% (466 of 1426) of patients had recurrence during follow-up of which 9.4% (135 of 1426) had local recurrences, 16.4% (234 of 1426) had distant recurrences, and 4.7% (67 of 1426) had both local and distant recurrences.

Gender, OBSTR (median survival time = 43; 95% CI = 33.9–52.1 months), PERF (median survival time 43; 95% CI = 22–64 months), OBS-PERF (median survival time = 29; 95% CI = 6.4–51.6 months), emergency operation performed, reoperation performed, number of major surgical complications, number of major medical complications, TNM stage, histologic grade, and venous invasion showed statistically significant differences for

Table 3 Five-year DFS probabilities in relation to demographics of patients and characteristics of treatment and tumor of 1426 patients with colorectal cancer who were treated with curative intent between 1984 and 2004

	Sample size; percent ($n = 1426$) (%)	5-year DFS rate	95% CI	p Value
Demographics, symptoms, and operation				
Age				0.732
<50 years	122; 8.6	60.5%	49.5, 71.5	
50–79 years	1084; 76.0	64.9%	61.6, 68.2	
≥80 years	220; 15.4	62.4%	54.8, 70.0	
Gender				0.006
Male	773; 54.2	60.8	56.7, 64.9	
Female	653; 45.8	67.9	63.8, 72.0	
Obstruction and perforation				<0.001
None (UNCOM)	1200; 84.2	67.7%	64.6, 70.8	
Obstruction only (OBSTR)	153; 10.7	47.5%	38.5, 56.5	
Perforation only (PERF)	53; 3.7	46.5%	30.6, 62.4	
Both (OBS-PERF)	19; 1.3	25.0%	1.7, 48.3	
Duration of initial symptoms				0.084
<1 month	245; 21.7	56.0	48.9, 63.1	
1 to <3 months	348; 30.9	59.4	53.5, 65.3	
3 to <6 months	240; 21.3	65.3	58.4, 72.2	
≥6 months	295; 26.2	63.2	56.5, 69.9	
Unknown $n = 298$				
Emergency operation				<0.001
No	1193; 83.7	67.1	64.0, 70.2	
Yes	233; 16.3	49.0	41.4, 56.6	
Number of major surgical complications[a]				0.002
0	1278; 89.6	65.4	62.5, 68.3	
1	111; 7.8	55.7	44.1, 67.3	
≥2	37; 2.6	42.0	24.0, 60.0	
Major medical complications[b]				0.002
0	1179; 82.7	66.2	63.1, 69.3	
1	171; 12.0	55.3	46.1, 64.5	
≥2	76; 5.3	45.8	30.9, 60.7	
Reoperation				<0.001
No	1324; 92.8	65.6	62.7, 68.5	
Yes	102; 7.2	44.5	32.7, 56.3	
Tumor characteristics				
Primary cancer site				0.308
Cecum	227; 15.9	66.6	59.7, 73.5	
Ascending colon	108; 7.6	68.8	58.8, 78.8	
Hepatic flexure	61; 4.3	60.7	46.6, 74.8	
Transverse colon	103; 7.2	64.3	53.3, 75.3	
Splenic flexure	55; 3.9	72.0	58.9, 85.1	
Descending colon	55; 3.9	60.5	46.0, 75.0	
Sigmoid colon	333; 23.4	67.3	61.6, 73.0	
Rectum	484; 33.9	59.7	54.4, 65.0	
Stage of tumor (TNM)				<0.001
I	275; 19.9	85.0	79.9, 90.1	
II	661; 47.9	70.1	66.0, 74.2	
III	444; 32.2	45.1	39.8, 50.4	

Table 3 continued

	Sample size; percent ($n = 1426$) (%)	5-year DFS rate	95% CI	p Value
Histologic type				0.479
Adenocarcinoma	1209; 84.8	64.2	61.1, 67.3	
Mucinous adenocarcinoma	215; 15.1	63.7	56.6, 70.8	
Signet ring	2; 0.1	100		
Venous invasion				<0.001
No	1255; 88.0	66.5	63.6, 69.4	
Yes	171; 12.0	46.9	38.3, 55.5	

95% CI = 95% confidence interval

[a] Major surgical complications included bowel complications needing reoperation, anastomosis dehisence, fistula, perineal sinus, intra-abdominal abscess needing reoperation, hemorrhage, and other complications needing reoperation

[b] Major medical complications included renal failure, respiratory complications, cardiac complications, DVT, pulmonary embolus, and CVA

Table 4 Operations performed on 1425 patients with colorectal cancer who were treated with curative intent between 1984 and 2004

Operation	No. of patients	Percentage of 1425
Right hemicolectomy	459	32.2
Segmental "sleeve" resection	11	0.8
Left hemicolectomy	65	4.6
Transverse colectomy	19	1.3
Hartman's procedure	69	4.8
Total colectomy with ileorectal anastomosis	59	4.2
Total colectomy with ileostomy	15	1.1
Sigmoid colectomy	108	7.6
Anterior resection	481	33.7
Anterior resection with colo-anal pull-through anastomosis	4	0.3
Abdominoperineal resection	125	8.8
Local transanal excision	10	0.7

One patient record had missing information on the type of operation

DFS comparing cumulative survival probabilities according to Kaplan-Meier (Table 3, Figs. 1 and 2). Compared with patients with symptoms, the 55 asymptomatic patients showed significantly improved DFS ($p = 0.024$). Other analyzed factors that did not show any differences in DFS according to Kaplan-Meier analyses were age, history of benign colon polyps, preoperative CEA level, pre- and postoperative radio- and or chemotherapy, primary cancer site, and histologic type.

Overall cancer recurrences were significantly higher in the OBSTR group (44.4%, $p < 0.001$) and the OBS-PERF group (57.9%, $p = 0.021$) compared with UNCOM (30.4%), but it was not significant in the PERF group (41.5%, $p = 0.095$). This was related to significantly higher distant recurrence rates in the OBSTR group (21.6 vs. 15.2%, $p = 0.046$), but significance was not reached in the PERF (24.5%, $p = 0.079$) and OBS-PERF groups (31.6%, $p = 0.099$). There were no significant differences in the local recurrence rates in the OBSTR (12.4%), PERF (9.4%), and OBS-PERF groups (21.1%) compared with the UNCOM group (8.9%). There were also no significant differences in the local and distant recurrence rates (in same patient) in the OBSTR (5.9%), PERF (5.7%), and OBS-PERF (15.8%) groups compared with the UNCOM group (4.3%).

Multivariable Cox proportional hazard analysis for DFS showed that TNM stage III ($p < 0.001$), poorly differentiated grading ($p = 0.018$), major medical complications ($p = 0.011$), the need for reoperation ($p = 0.018$), OBS-PERF ($p = 0.008$), and venous invasion ($p = 0.002$) were independently associated with cancer recurrence (Table 6).

Discussion

We analyzed data from 1426 patients who underwent potentially curative colorectal cancer surgery from 1984 to 2004 with a median follow-up of 45 (IQR = 19–72) months. During that period of time the proven value for adjuvant therapy had only gradually become confirmed. Not surprisingly, 94.6% of colon cancers did not undergo any chemotherapy. Although these data may not be completely applicable to present management, they may still be valuable, particularly where adjuvant therapy is not possible because of a patient's comorbidities, social or geographical circumstances, and choice. Furthermore, surgery remains the primary treatment for colorectal cancer in most circumstances [19]; therefore, factors important to the outcome unlikely were totally altered by adjuvant therapy. In this context, we found that colorectal cancer DFS was worse with OBS-PERF. The other independent factors found to affect DFS were medical complications and

Table 5 Postoperative complication rates

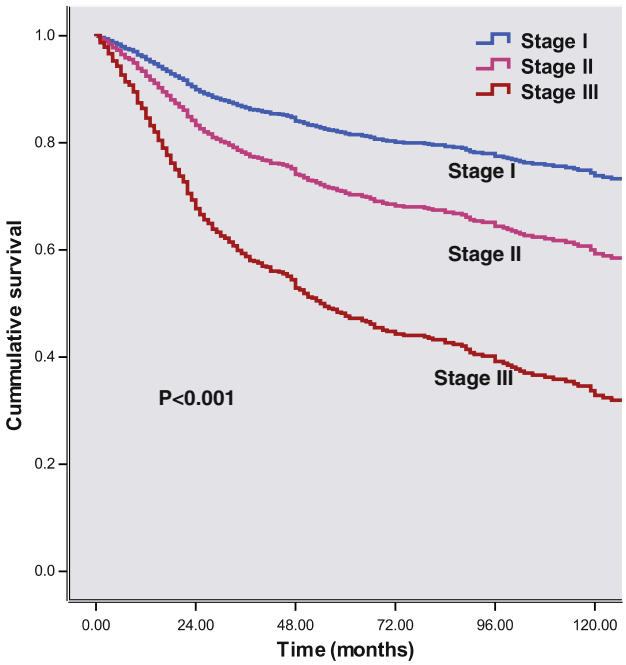
	Percent of all patients ($n = 1426$)	Percent of all patients with medical complications ($n = 248$)
Major medical complications ($n = 247$)	17.3	99.6
Renal failure ($n = 37$)	2.6	14.9
Respiratory complications ($n = 175$)	12.3	70.6
Cardiac ($n = 108$)	7.6	43.5
DVT ($n = 16$)	1.1	6.6
Pulmonary embolus ($n = 17$)	1.2	6.9
Cerebrovascular accidents ($n = 9$)	0.6	3.6
Minor medical complication (enterocolitis) ($n = 1$)	0.1	0.4
	Percent of all patients ($n = 1426$)	Percent of all patients with surgical complications ($n = 464$)
Major surgical complications ($n = 148$)	10.4	31.9
Bowel complications requiring reoperation		
Total ($n = 29$)	2.0	6.3
Small bowel obstruction ($n = 13$)	0.9	2.8
Large bowel obstruction ($n = 2$)	0.1	0.4
Small and large bowel obstruction ($n = 2$)	0.1	0.4
Paralytic ileus ($n = 22$)	1.5	4.7
Anastomic leak ($n = 72$)	5.0	15.5
Fistula ($n = 20$)	1.4	4.3
Perineal sinus ($n = 14$)	1.0	3.0
Intra-abdominal abscess requiring reoperation ($n = 23$)	1.6	5.0
Hemorrhage requiring reoperation ($n = 16$)	1.1	3.4
Minor surgical conditions ($n = 316$)	22.2	68.1
Wound infection ($n = 191$)	13.4	41.2
Bowel complications, no reoperation		
Total ($n = 134$)	9.4	28.9
Small bowel obstruction ($n = 16$)	1.1	3.4
Large bowel obstruction ($n = 2$)	0.1	0.4
Small and large bowel obstruction ($n = 1$)	0.07	0.2
Paralytic ileus ($n = 105$)	7.4	22.6
Intra-abdominal abscess not requiring percutaneous drainage or reoperation ($n = 23$)	1.6	5.0

DVT deep venous thrombosis

Results were based on 1426 patients with colorectal cancer who were treated with curative intent between 1984 and 2004. One patient could have had more than one complication

histopathologic criteria such as advanced TNM staging, tumor venous invasion, and poor differentiation grading. Major medical complications were those that were potentially life-threatening, evoking significant systemic inflammatory response which increases early postoperative morbidity and compromises long-term survival [20–23].

The DFS in our patients was related to total cancer recurrence rate (33%) consisting of 9.4% local recurrence alone, 16.4% distant recurrence alone, and 4.7% local and distant recurrence in the same patient. The skill of the surgical management team can affect recurrence rates and other outcomes [19, 24]. Nonetheless, Staib et al. [16] reported from a one-institution series over a comparable time period an overall cancer recurrence rate of 27%. This rate comprised 3.4% local recurrence, 6.6% distant recurrence, and 15% local and distant recurrence. Local recurrence is related to tumor grading and staging [24, 25], which is consistent with our findings described above. It is



Number of recurrences by time of disease free survival and by TNM stage.

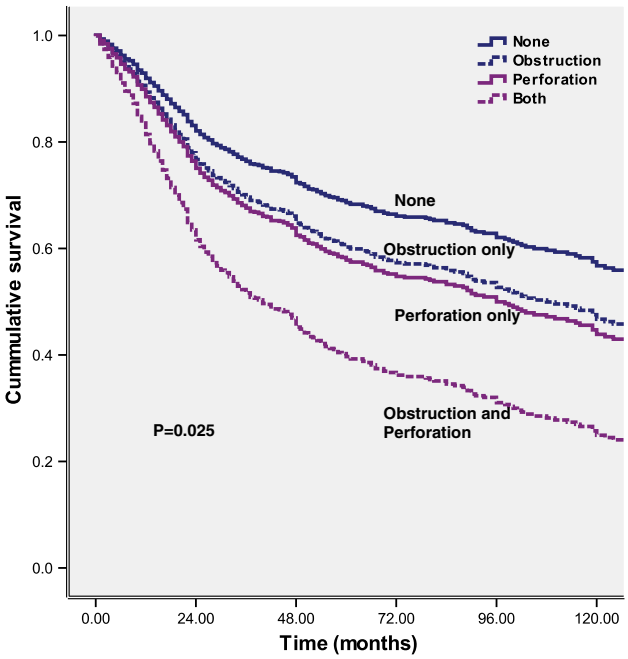
	Disease free survival (months)					
	0-23	24-47	48-71	72-95	95-119	>=120
TNM stage I	19 of 86 (22.1%)	8 of 46 (17.4%)	4 of 72 (5.6%)	4 of 28 (14.3%)	3 of 18 (16.7%)	2 of 25 (8.0%)
TNM stage II	95 of 222 (42.8%)	42 of 119 (35.3%	28 of 154 (18.2%)	5 of 58 (8.6%)	7 of 36 (19.4%)	5 of 72 (6.9%)
TNM stage III	130 of 199 (65.3%)	56 of 90 (62.2%)	21 of 69 (30.4%)	7 of 33 (21.1%)	7 of 22 (31.8%)	4 of 31 (12.9%)

Fig. 1 Disease-free cumulative survival probabilities estimated by Cox proportional hazard regression and stratified by TNM staging

interesting that our analysis found no difference in DFS between colon and rectal cancers. The local relapse probability, metastatic pattern, surgery, and multimodal management have suggested that colon cancers may be different from rectal cancers [19]. Other reports showed no differences in local recurrence rates between colon cancer and rectal cancer [24–26], suggesting that with proper total mesorectal excision techniques, the surgical oncologic clearance for rectal cancers should well approach that for colon cancers [24, 25].

OBS-PERF is a relatively rare complication which may explain why it has not been studied previously as an independent high-risk entity. It comprises 1.3% of our colorectal cancer patients ($n = 19$), where the poorer DFS was due to higher overall recurrence rates. The long-term prognosis for OBS-PERF patients remains controversial, with relatively sparse data available [6, 7, 27]. DFS may be affected by the site of the perforation, i.e., whether proximal to the obstructing cancer or at the site of the obstructing cancer. In most of our OBS-PERF patients, a Hartmann resection was performed as applicable to a perforation at the site of the obstructing cancer, which may be different from the perforation at the right colon due to obstruction from a left-sided cancer described in the other series. Perforation at the site of the cancer in the presence of obstruction may lead to an explosive effect, with dissemination of cancer cells.

In our database the acuteness of the symptoms recorded was probably a more accurate indicator of the "emergency" nature of the procedures performed. Many procedures that would have otherwise been "emergency" surgery had probably not been classified as such because it had often been arranged to perform the operations on the next available elective list after proper resuscitation. Hence, OBSTR patients had significantly shorter symptom duration and were likely—but not totally—classified as emergency operations. Our OBSTR patients were older; consistent with reports that older patients were more likely to have emergency surgery [4, 27–30], advanced cancers, and comorbidities, including cardiovascular and respiratory



Number of recurrences by time of disease free survival and by obstruction, perforation, or both.

	Disease free survival (months)					
	0-23	24-47	48-71	72-95	95-119	>=120
None (UNCOM)	179 of 402 (44.5%)	78 of 205 (38.0%)	47 of 261 (18.0%)	16 of 110 (14.5%)	17 of 66 (25.8%)	10 of 108 (9.3%)
Obstruction only (OBSTR)	38 of 60 (63.3%)	18 of 30 (60.0%)	5 of 23 (21.7%)	0 of 8 (0%)	0 of 9 (0%)	1 of 14 (7.1%)
Perforation only (PERF)	14 of 27 (51.9%)	5 of 10 (50.0%)	0 of 7 (0%)	0 of 1 (0%)	0 of 1 (0%)	0 of 4 (0%)
Obstruction & Perforation (OBS-PERF)	7 of 11 (63.3%)	3 of 4 (75.0%)	1 of 1 (100%)	/	/	0 of 2 (0%)

Fig. 2 DFS probabilities estimated by Cox proportional hazard regression and stratified by obstruction, perforation, and obstruction and perforation

dysfunction [4, 29, 31]. Not surprisingly, emergency surgery for OBSTR and PERF colorectal carcinoma has been documented to carry high rates of morbidity and mortality [32, 33]. In our patients, the 30-day mortality of 1.5% is comparable to the 0.8% reported previously [16, 34], and the morbidity of 40.8% is comparable to the 18-37% reported previously.

Earlier studies of relatively small numbers of patients suggested that OBSTR was associated with high mortality rates but had a long-term survival rate similar to that of UNCOM [35]. However, other studies, including population-based ones, have shown poorer survival at 5 years after emergency resection in excess to the effect of perioperative mortality [14, 32] and that cancer-related survival was also adversely affected [2, 8]. OBSTR was associated with a higher total cancer recurrence rate, mainly because of a higher incidence of distant systemic recurrences. Carraro et al. [16] reported that after one-stage emergency curative surgery, patients with OBSTR had worse survival and higher risk of metastatic disease compared to UNCOM.

PERF has been reported to have poorer overall survival and cancer-related survival [17] and higher local recurrence rates [18]. Others have reported PERF cancers to have recurrence rates, overall survival, and DFS*** comparable to those of OBSTR cancers [7, 36]. In our series, it was likely that minor locally sealed off perforations included in the PERF analysis were adequately dealt with according to merits in a dedicated specialist unit. Therefore, our findings would be consistent with the report of Kagda et al. [37] that if clear oncologic margins can be obtained at operation, the prognosis of locally contained perforated rectal cancers approaches that of a potentially

Table 6 Results of multivariable Cox proportional hazard model analyzing 1364[a] patients for DFS who were treated for colorectal cancer with curative intent between 1984 and 2004

Prognostic factor	Sample size ($n = 1364$)	DFS (%)	Relative risk (95% CI)	*P* Value
TNM stage				
I	273	14.7	1	
II	653	27.4	1.7 (1.2, 2.4)	0.003
III	438	50.2	3.5 (2.5, 4.9)	<0.001
Obstruction and perforation				
No (UNCOM)	1152	30.1	1	
Obstruction only (OBSTR)	144	43.1	1.3 (0.97, 1.9)	0.077
Perforation only (PERF)	50	38.0	1.5 (0.90, 2.3)	0.123
Both (OBST-PERF)	18	61.1	2.5 (1.3, 4.8)	0.008
Venous invasion				
No	1201	30.5	1	
Yes	163	44.8	1.5 (1.2, 2.0)	0.002
Histologic grade of tumor				
Well/moderately differentiated	1185	30.7	1	
Poorly differentiated	179	41.9	1.4 (1.1, 1.7)	0.018
Major medical complications[b]				
0	1292	32.2	1	
≥ 2	72	31.9	1.8 (1.1, 2.7)	0.011
Reoperation				
No	1267	31.3	1	
Yes	97	44.3	1.5 (1.1, 2.1)	0.018

95% CI = 95% confidence interval

[a] Sample size was reduced from 1426 to 1364 because of missing values for TNM stage, preoperative hemoglobin, perforation, and histologic grade. The model was adjusted for the confounding effects of gender, emergency operation performed, preoperative hemoglobin, urinary symptoms, and site of primary tumor

[b] Major medical complications included renal failure, respiratory complications, cardiac complications, DVT, pulmonary embolus, and CVA

curative resection. Cheynel et al. [38] found that after exclusion of operative mortality, PERF no longer had any significant effect on a poorer prognosis.

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