Early postoperative outcome after curative colorectal cancer surgery

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ABSTRACT

Introduction: Colorectal cancer is uncommon in the Indian subcontinent, so there is a paucity of outcome data from this region. The aim of our study was to identify risk factors for early postoperative morbidity and mortality following curative colorectal cancer surgery in our set-up.

Methods: The data on patients with pathologically confirmed colorectal cancer who underwent curative surgery at Aga Khan University Hospital, Karachi, Pakistan, between January 1999 and December 2008 were recorded. Patients who developed early postoperative morbidity or mortality were compared with those who followed a healthy course after surgery.

Results: A total of 250 consecutive patients underwent colorectal cancer surgery during the study period. Postoperative complications were found in 34.8 percent of the patients, out of which four deaths occurred. Serum albumin level less than 3.5 g/dl (odds ratio [OR] 3.75, 95 percent confidence interval [CI] 1.37–10.23) and tumours involving the left colon (OR 2.60, 95 percent CI 1.02–6.64) were identified as independent risk factors for early postoperative complications on multivariate analysis.

Conclusion: A low serum albumin level and the presence of a left-sided colonic tumour were significant risk factors for early postoperative complications. Information on these complications and the risk factors for early postoperative outcome is an important consideration for patients and surgeons.

Keywords: colorectal cancer, outcome, risk factors

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INTRODUCTION

Colorectal cancer is the second most common malignancy in the developed world and in some parts of Asia, but it is relatively uncommon in South Asia, particularly the Indian subcontinent.[1,2] Surgical resection is the mainstay of treatment for patients with non-metastatic colorectal carcinoma.[3] About 90% of patients with colorectal cancer require surgery, which is usually carried out with a curative intent.[4] Despite refinements in surgical techniques, bowel preparation patterns, prophylactic antibiotics and postoperative care, colorectal surgery is associated with a 3%–6% mortality rate and a 20%–40% morbidity rate.[5,6] The situation is further complicated by the fact that colorectal cancer is a disease of the elderly, with only 5% of cases recorded among those below 40 years of age.[7,8] The identification of risk factors and optimised preoperative care of colorectal carcinoma patients may play a role in improving early postoperative outcomes.

A number of previous studies have documented the morbidity and mortality rates after colorectal surgery. Although some initial studies from high-volume centres in the West suggested a correlation between the hospital and the surgeon's volumes and long-term outcome after colorectal surgery,[9,10] the results of other recent systematic reviews are not supportive of this view.[11] Geographic variations in the incidence of colorectal cancer have been described,[1,12] but there is a scarcity of outcome data originating from South Asian countries. Our institution is a tertiary care university hospital located in a low incidence zone for colorectal cancer.[1,12] The aim of our study was to determine the postoperative complication rate and the risk factors responsible for early postoperative morbidity and mortality following curative colorectal cancer surgery.

METHODS

Patients with pathologically confirmed colorectal cancer who underwent primary surgery at Aga Khan University Hospital, Karachi, Pakistan, between January 1999 and December 2008 were identified by the Department of Health Management and Information System. The clinical and pathologic characteristics of these patients were recorded with the help of a detailed questionnaire, which included the patients' demographics, associated comorbid conditions, American Society of Anaesthesiologists (ASA) score, serum albumin levels

Table I. Demographic features and clinical presentation of patients in both groups.

Variable	No. (%)		p-value
	Group A (n = 87)	Group B (n = 163)	
Mean age ± SD	54.4 ± 16.5	55.3 ± 14	0.91
Gender			0.27
Male	61 (70.1)	103 (63.1)	
Female	26 (29.8)	60 (36.9)	
Hypertension	28 (32.1)	57 (34.9)	0.65
Diabetes mellitus	11 (12.6)	24 (14.7)	0.65
History of ischaemic heart disease	17 (19.5)	22 (13.9)	0.21
Weight loss	20 (22.9)	35 (21.4)	0.78
Bleeding per rectum	46 (52.8)	69 (42.3)	0.11
Abdominal pain	46 (52.8)	89 (54.6)	0.15
Obstruction	10 (11.4)	15 (9.2)	0.56

SD: standard deviation

Table II. Postoperative complications that developed after curative colorectal cancer surgery (n = 250).

Postoperative complications	No. (%)
Surgical complications	
Surgical site infection	
Superficial	42 (16.8)
Deep	3 (1.2)
Abdominal complications	
Anastomotic leak	8 (3.2)
Abdominal sepsis/abscess	7 (2.8)
Paralytic ileus	4 (1.6)
Persistent diarrhoea	4 (1.6)
Intestinal obstruction	1 (0.4)
Systemic complications	
Genitourinary	
Urinary tract infection	14 (5.6)
Difficulty in voiding	16 (6.4)
Respiratory	
Pleural effusion	8 (3.2)
Pneumonia	7 (2.7)
Cardiovascular	
Myocardial infarction	3 (1.2)
Atrial fibrillation	1 (0.4)
Others	
Systemic sepsis	9 (3.6)
Stroke	1 (0.3)

for nutritional status, mode of admission (elective or emergency), site of tumour (descending colon and rectosigmoid tumours were grouped together as left-sided colonic tumours, whereas caecum, ascending colon and transverse colon tumours were considered right-sided colonic lesions), TNM staging and the number of lymph nodes that were positive for tumour metastasis. Patients who developed early postoperative morbidity or mortality were identified (Group A) and compared with those who followed a healthy recovery course after surgery (Group B). Early postoperative morbidity was defined as any untoward event developing within 30 days of surgery that changed the usual course of recovery. Patients who presented with perforation and those who underwent only palliative surgical treatment were excluded from the study.

The data obtained was analysed using the Statistical Package for the Social Sciences version 16.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were computed for the characteristics of the patients, laboratory parameters, tumour attributes and postoperative morbidity and mortality. Univariate analysis was carried out by computing the odd ratios (OR) and 95% confidence interval (CI) to compare the two groups for each potential risk factor. Multivariate analysis was carried out to identify risk factors that were independently associated with early morbidity, which included factors found to be significant on univariate analysis.

RESULTS

A total of 250 consecutive patients underwent colorectal cancer surgery with a curative intent during the study period, out of which 87 (34.8%) patients developed early postoperative complications (Group A) and 163 (65.2%) followed a healthy recovery course post surgery (Group B). The procedures included right hemicolectomy or right extended hemicolectomy in 84 (33.6%) patients, transverse colectomy in three (1.2%), left hemicolectomy in 21 (8.4%), sigmoid colectomy in 31 (12.4%), anterior or low anterior resection in 42 (16.8%), abdominoperineal resection in 54 (21.6%) and total or sub-total colectomy in 15 (6%) patients. After excluding patients who underwent an abdominoperineal resection, a diverting stoma was fashioned in 37 (18.8%) patients. Excluding patients with stomas, 88 (55.3%) patients underwent hand-sewn anastomosis and 71 (44.7%) had stapled anastomosis.

Table I summarises the demographics and clinical characteristics of the patients in Group A (n = 87) and Group B (n = 163). The proportion of male patients was slightly higher in Group A (70%) as compared to Group B (63%). Hypertension and diabetes mellitus were common comorbid conditions, and the distribution was similar in the two groups. Preoperative obstruction was more frequently observed in Group A patients (11.4%).

The details of the postoperative complications encountered are shown in Table II. A total of 128 postoperative complications were recorded in 87 (34.8%) patients, including four (1.6%) deaths. The cause of death was postoperative abdominal sepsis, resulting in septic shock for two patients. One patient

Table III. Association of related variables with development of early postoperative complications using univariate analysis.

Variable	No. (%)		OR	95% CI	p-value
	Group A (n = 87)	Group B (n = 163)			
Age (yrs)					
< 65	60 (69.0)	119 (73.0)			
> 65	27 (31.0)	44 (27.0)	1.217	0.68–1.21	0.50
Gender					
Female	26 (29.9)	60 (36.8)			
Male	61 (70.1)	103 (63.2)	1.367	0.78–2.38	0.27
Presence of comorbidity					
No	43 (49.4)	74 (45.4)			
Yes	44 (50.6)	89 (54.6)	1.175	0.69–1.98	0.54
Charlson index score					
≤ 2	57 (65.5)	122 (74.8)			
≥ 3	30 (34.5)	41 (25.2)	0.639	0.36–1.12	0.12
ASA score					
< 2	61 (70.1)	111 (68.1)			
> 2	26 (29.9)	52 (31.9)	0.910	0.51–1.60	0.74
Mode of presentation					
Elective	77 (88.5)	148 (90.8)			
Emergency	10 (11.5)	15 (9.2)	1.92	0.91–4.05	0.08
Albumin (g/dl)*					
≥ 3.5	7 (8.0)	29 (17.7)			
< 3.5	27 (31.0)	36 (22)	3.107	1.18–8.15	0.02
Site of tumour					
Right colon	22 (25.3)	62 (38)			
Left colon	65 (74.7)	101 (62)	1.814	1.01–3.23	0.04
Type of anastomosis (n = 159)					
Hand-sewn	31 (35.6)	57 (34.9)			
Stapled	23 (26.4)	48 (29.4)	1.135	0.58–2.20	0.708
Lymph node involvement					
< 15 +ve for metastasis	48 (55.2)	80 (49.1)			
> 15 +ve for metastasis	39 (44.8)	83 (50.9)	0.783	0.46–1.32	0.35
Stage of tumour (TNM)					
Stage 1 & 2	54 (62.1)	98 (60.1)			
Stage 3 & above	33 (37.9)	65 (39.9)	1.08	0.63–1.85	0.76
Stoma formation (n = 91)	33 (37.9)	58 (35.6)	0.90	0.52–1.54	0.71

OR: odds ratio; CI: confidence interval; ASA: American Society of Anaesthesiologists; TMN: tumour, node, metastasis
* Data is missing for 151 patients.

presented with colonic obstruction and developed systemic sepsis with adult respiratory distress syndrome after surgery, while another patient with myelofibrosis developed coagulopathy after surgery, which resulted in intracerebral haemorrhage and death. Surgical complications were noted in 58 (23.2%) patients and systemic complications, in 46 (18.4%) patients. 17 (6.8%) patients developed both surgical and systemic complications. More than one surgical and systemic complication was observed in 11 and 15 patients in Groups A and B, respectively. The overall incidence of surgical site infection was 18%, and the majority of these were superficial infections. The incidence of intra-abdominal complications was 9.6% and 3.5% of the patients required a repeat operation.

Univariate analysis was first conducted using the perioperative variables to explore the potential risk factors for postoperative complications, as shown in Table III. A multivariate logistic regression model was then developed for variables that were found to be significant in the univariate analysis. Table IV presents the multivariate model of risk factors that were independently associated with early postoperative complications. Serum albumin levels < 3.5 g/dl (OR 3.75, 95% CI 1.37–10.23) and a tumour involving the left colon (OR 2.60, 95% CI 1.02–6.64) were independent risk factors for early postoperative complications.

DISCUSSION

A number of studies from high incidence zones in the West have documented early postoperative outcomes after colorectal surgery. Although few of these studies have addressed patients with colon and rectal cancer only,[10] others have combined benign and malignant diseases to determine the overall outcome.[13] Despite the recently questionable association between surgeon

Table IV. Multivariate logistic regression model of risk factors associated with development of early postoperative complications.

Variable	Adjusted OR	95% CI
Site of tumour		
Right-sided	Reference	
Left-sided	2.60	1.02–6.64
Albumin level (g/dl)		
≥ 3.5	Reference	
< 3.5	3.75	1.37–10.23

OR: odds ratio; CI: confidence interval

and hospital volume for colorectal surgery,[11] there is a scarcity of data on early outcomes after colorectal cancer surgery from low-volume centres, especially in South Asia. In the absence of cancer registries and population-based data from developing countries in low incidence zones, the outcome data from a single institution database becomes more significant.

Our institution is a tertiary care university hospital in which gastrointestinal oncological procedures are mainly performed by general surgeons, and subspecialisation occurs in the early phase of development. The perioperative care of the patients at our hospital is fairly standardised for elective surgery, except for the fact that preoperative bowel preparation is dictated by the operating surgeon. The patient may receive no bowel preparation at all or mechanical bowel washout only. All patients were administered three doses of empiric antibiotics for wound prophylaxis and subcutaneous heparin for deep venous thrombosis prophylaxis. Due to a lack of expertise and infrastructure for laparoscopy, surgery is usually performed through an open approach. The choice of hand-sewn or stapled anastomosis is made by the operating team. The facility of endoluminal stenting for obstructing tumours is not routinely utilised due to the unavailability of the required resources. After surgery, the patients are usually nursed in special care units, with invasive monitoring and daily rounds by physiotherapists and stoma care nurses. The patients are encouraged to aim for early mobilisation and are transferred to the ward once they are reasonably optimised. A liquid diet is instated once patients have active bowel sounds, and they gradually progress to a regular diet.

The 30-day mortality rate of 1.6% found in our study is comparable to that reported in the literature from high-volume centres.[5,6] Most of our patients required emergency surgery, and emergency colorectal surgery has been shown to be associated with poor outcome, with operative mortality rates reportedly as high as 20% in some series.[6,14,15]

The 34.8% incidence rate of early postoperative complications found in our study is also comparable to most of the published data.[5,6,13] The commonest surgical complication encountered among our patients was surgical site infection (SSI). The SSI rate of 17.8% found in our study is higher than that in other studies.[16,17] A number of risk factors have been identified in the literature for the development of SSI after colorectal surgery,[16] but one significant factor among our patients was the absence of an ongoing surveillance system for SSI at our hospital. Continuous surveillance with regular feedback and improvement has been shown to reduce SSI rates even in developing countries.[18]

Low serum albumin levels and the presence of left-sided tumours were identified as independent risk factors for early postoperative complications by multivariate analysis in our study. Approximately 31% of patients in Group A had an albumin level below 3.5 g/dl as compared to 22% of patients in Group B. Albumin has a long half-life of 20 days, and the metabolic effects on its concentration reflect prolonged malnourishment, as seen in cancer patients. Patients with colorectal cancer are at risk of malnutrition due to cancer-induced hypermetabolism, dietary intake reduction and cancer cachexia.[19,20] Cancer patients also have increased whole protein turnover and subsequent body nitrogen loss.[21] Hypoalbuminaemia is widely accepted as a good indicator of malnutrition in many cancer studies.[22,23] It has also been shown to be associated with poor tissue healing, decreased collagen synthesis in surgical wounds and the site of anastomosis,[24,25] and impairment of immune responses such as macrophage activation and granuloma formation.[26] A common explanation of the association between serum albumin level and postoperative septic complications is the argument that serum albumin is a marker of circulating visceral protein,[27] and a direct measure of nutritional and immunological status. Therefore, hypoalbuminaemia predisposes patients not only to surgical complications such as SSI and poor anastomotic healing, but also to remote infections like pneumonia. A recent case-control study from the United States has also reported that low serum albumin is an independent risk factor for anastomotic leak after colorectal surgery.[28]

Patients with rectal cancer were included among those with left-sided colonic tumours in our study. Although recent data suggests that the incidence of right-sided colonic tumours is increasing,[29] the majority of patients (66%) in our study had a left-sided tumour. Out of a total of 166 patients with left-sided tumours, 65 patients developed postoperative complications, and this

comprised 75% of all the cases in Group A. According to some studies,[30] obstruction is a common presentation (8%–29%) in left-sided colorectal cancers and the most common cause of emergency surgery among these patients. Overall, 31 patients in our study presented with colonic obstruction and 25 of them had a left-sided tumour. These complicated situations require emergency surgery, which results in high rates of morbidity.[14,15] A recent study from Asia comparing the outcome between left- and right-sided tumours has suggested that patients with left-sided tumours present more frequently with obstruction and have higher rates of morbidity and mortality.[31] Our data further strengthens the view that patients with left-sided colonic tumours require emergency surgery more frequently, which leads to higher rates of postoperative complications.

Although the data of other studies has suggested that the extent of nodal dissection may have an impact on long-term survival,[29] we did not observe any effect of lymph node metastases (> 15 nodes) on the short-term outcome. Similarly, the overall stage of the disease also failed to have any significant impact on the short-term outcome in our study (Stage 1 and 2 vs. Stage 3 and 4). In summary, the results of our study indicate that the mortality and morbidity rates after curative colorectal cancer surgery in our study are comparable to the published data, and that such oncological surgery can be performed with a reasonable level of safety in low-volume centres. Despite the limitations of this being a retrospective study, the results are important due to the limited data available from developing countries in low incidence zones like ours. The way forward could involve prospective data collection and the development of cancer registries with pooling of the data from major oncological institutions. We have identified preoperative hypoalbuminaemia and the presence of left-sided tumours as the two independent risk factors for early postoperative complications and mortality following colorectal cancer surgery in our set-up. Knowledge of the incidence and risk factors for early postoperative outcome may provide patients and surgeons from low-volume centres located in low incidence zones with important information regarding colorectal carcinoma.

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