



Original research

The relationship between systemic inflammation and stoma formation following anterior resection for rectal cancer: A cross-sectional study



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HIGHLIGHTS

- Postoperative inflammatory response associated with morbidity following colorectal surgery.
- No association with temporary stoma formation following anterior resection for rectal cancer.
- Both inflammatory response and complications were associated with permanent stoma.

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ABSTRACT

Introduction: There is evidence that temporary defunctioning stoma formation in patients undergoing anterior resection reduces the risk of anastomotic leakage. The aim of the present study was to investigate the relationship between stoma formation, the postoperative systemic inflammatory response and complications following anterior resection for rectal cancer.

Methods: Data was recorded prospectively for patients who underwent anterior resection for histologically proven rectal cancer, from 2008 to 2015 at a single centre, $n = 167$. Patients had routine preoperative and postoperative blood sampling including serum C-reactive protein (CRP). Postoperative complications including anastomotic leakage were recorded.

Results: Of the 167 patients, the majority were male (61%) and over 65 years old (56%) with node negative disease (60%). 36 patients (22%) underwent preoperative neoadjuvant treatment. 100 patients (60%) had a stoma formed at the time of surgery. Stoma formation was significantly associated with male sex (69% vs. 50%, $p = 0.017$), neoadjuvant chemoradiotherapy (30% vs 9%, $p = 0.001$) and open surgery (71% vs. 55%, $p = 0.040$). Of those 100 patients who had a stoma formed, 80 had it reversed. Permanent stoma was significantly associated with increasing age ($p = 0.011$), exceeding the established CRP threshold of 150 mg/L on postoperative day 4 (67% vs 37%, $p = 0.039$), higher incidence of postoperative complications (76% vs 47%, $p = 0.035$), anastomotic leakage (24% vs 2%, $p = 0.003$) and higher Clavien Dindo score ($p = 0.036$).

Conclusions: There was no significant association between stoma formation during anterior resection and the postoperative systemic inflammatory response. However, in these patients both the postoperative systemic inflammatory response and complications were associated with permanent stoma.

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1. Introduction

Rectal cancer is one of the most prevalent cancers diagnosed in the Western world [1]. Anterior resection with total mesorectal excision (TME) is the preferred surgical technique, to preserve the anal sphincter and avoid a permanent colostomy where abdominoperineal resection is not required [2]. However, anterior resection is associated with increased risk of anastomotic leakage, a major complication of this type of rectal surgery, when compared to

resection of colorectal cancer in other locations [3]. Furthermore, anastomotic leakage has been indicated to be associated with increased risk of local recurrence and decreased short and long term survival of patients who have undergone potentially curative resection [4,5].

Recent evidence suggests that the postoperative systemic inflammatory response, measure by C-reactive protein (CRP), is important in both short and long term outcomes of colorectal patients and that it may be a causal factor in development of postoperative complications [6–10]. A recent comprehensive review has suggested that CRP concentrations exceeding 150 mg/L on postoperative days 3–5 should alert clinicians to the possible development of postoperative complications, including anastomotic leakage, precluding early discharge [11].

Several studies have suggested that construction of a defunctioning stoma in patients who are undergoing anterior resection reduces the incidence of postoperative complications, including anastomotic leakage, and reoperation [12–14]. Although it has traditionally been thought that this reduction in anastomotic leak rate is due to diversion of the faecal stream, it may be that the formation of a stoma attenuates the magnitude of the postoperative systemic inflammatory response and that it is through this mechanism by which they reduce the rate of postoperative complications.

Therefore, the aim of the present study was to investigate the relationship between defunctioning stoma formation, and reversal, the magnitude of the postoperative systemic inflammatory response, and complications in rectal cancer patients who have undergone anterior resection.

2. Patients and methods

2.1. Patients

Patients with histologically proven rectal cancer, who underwent anterior resection, between February 2008 and April 2015 at a single centre were included in the study. Patients who underwent emergency surgery, palliative procedures, or who had existing inflammatory conditions were excluded. Neoadjuvant treatment was offered to patients with histologically proven, locally advanced (T3–T4, borderline operable or inoperable) rectal tumours following discussion at a multi-disciplinary colorectal oncology meeting.

All patients received prophylactic antibiotics and venous thromboprophylaxis prior to the induction of anaesthesia as per hospital policy. All patients had a primary anastomosis formed and the decision to form a proximal defunctioning stoma, with temporary intent, was at the discretion of the operating surgeon. Patients had routine preoperative blood sampling including a full blood count (FBC), serum CRP and albumin concentration.

On each postoperative day patients were clinically assessed and had blood samples, including serum CRP, obtained routinely until discharged. Further postoperative investigation and intervention was at the discretion of the patient's surgical team who were not blinded to blood results. This study was approved by the West of Scotland Research Ethics Committee.

2.2. Methods

Data was collected prospectively in a database, anonymised, and subsequently analysed retrospectively. Recorded information included patient demographics, clinicopathological, operative data, postoperative data, and date of stoma reversal if applicable.

Serum concentrations of CRP (mg/L) were measured using an autoanalyzer (Architect; Abbot Diagnostics, Maidenhead, UK) with a lower detectable limit of 0.2 mg/L as was serum albumin (normal

range 35–50 g/L). The preoperative modified Glasgow Prognostic Score (mGPS) was calculated in patients for whom serum CRP and albumin concentrations were available [15]. Exceeding the established postoperative CRP threshold of 150 mg/L on postoperative days 3 or 4 was recorded [11].

Postoperative complications were recorded up to and including the first follow up clinic, usually 6 weeks after discharge from hospital. Infective complications were categorised as described elsewhere and summarised here briefly [8]. Wound (superficial surgical site) infection was defined as the presence of pus either spontaneously discharging from the wound or requiring drainage. Deep surgical site infection was defined as surgical or image-guided drainage of intra-abdominal pus. Anastomotic leak was defined as radiologically verified fistula to bowel anastomosis or diagnosed at laparotomy. Pneumonia was defined by fever above 38.5 °C and consolidatory chest X-ray findings requiring antibiotic treatment. Septicaemia was defined by the presence of sepsis combined with positive blood culture. Urinary tract infection was only included if complicated by septicaemia and confirmed with positive urine culture. Complications were also classified by severity using the Clavien Dindo grade [16].

2.3. Statistical analysis

Categorical data were compared using the Chi square test. Continuous data were non-normal so were displayed as medians and ranges, and were compared using the Mann-Whitney *U* test. Significant differences were found in the rate of defunctioning stoma formation dependent on whether a laparoscopic or open surgical approach was used and so a post hoc subgroup analysis was performed in those patients who underwent open surgery. Binary logistic regression of factors associated with permanent stoma was performed using a backward conditional model with removal of terms with $p > 0.05$ at each step. Statistical analyses were performed using IBM SPSS version 22 for Windows (Chicago, IL, USA). Two tailed p values < 0.05 were considered statistically significant. Missing data were excluded from analysis.

3. Results

3.1. Patients

After exclusion of those patients who underwent emergency or palliative surgery, or with existing inflammatory disease, 869 resections for colorectal cancer were performed during the study period, with 251 patients undergoing surgery for rectal cancer, of which 167 patients underwent anterior resection and were included in the study. The majority were male (102, 61%), over 65 years old (93, 56%) and underwent open surgery (109, 65%). 36 patients (22%) underwent neoadjuvant chemoradiotherapy. 7 patients (4%) had metastatic disease at the time of surgery, all located in the liver, of which 4 underwent synchronous resection, and 3 underwent staged liver resection following anterior resection. 79 patients (47%) developed a postoperative complication of which 73 were infective. There were 12 reported anastomotic leaks (7%). There were 3 deaths (2%) within the immediate postoperative period. Of the 79 patients who developed a postoperative complication, 61 were Clavien Dindo grade 1–2 and 18 were Clavien Dindo grade 3–5. 100 (60%) patients who underwent anterior resection had a defunctioning stoma formed.

3.2. Variables associated with stoma formation

Defunctioning stoma formation (Table 1) was significantly associated with male sex (69% vs. 50%, $p = 0.017$), neoadjuvant

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