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Original research

Colonic diverticulitis in chemotherapy patients: Should operative indications change? A retrospective cohort study

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HIGHLIGHTS

- Severity of diverticulitis was not associated with recent chemotherapy.
- Chemotherapy was safely resumed in most patients after acute diverticulitis resolved with medical management.
- Recurrent diverticulitis was not more common in cancer patients who were actively receiving chemotherapy.
- Recurrent diverticulitis was more likely to be complicated and lead to surgery in patients on chemotherapy.
- Interval colon resection after single episode of diverticulitis is not routinely indicated in these patients.

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ABSTRACT

Introduction: Management of the immunosuppressed patient with diverticular disease remains controversial. We report the largest series of colon cancer patients undergoing chemotherapy and hospitalized for acute diverticulitis, to determine whether recent treatment with systemic chemotherapy is associated with increased risk for/increased severity of recurrent diverticulitis. **Methods**: Retrospective cohort study of adult patients hospitalized for an initial episode of acute colonic diverticulitis at Memorial Sloan Kettering Cancer Center, 1988–2004. Outcomes in patients receiving systemic chemotherapy within one month of admission for diverticulitis ("Chemo") were compared to outcomes of patients not receiving chemotherapy within the past month ("No-chemo"). **Results**: A total 131 patients met inclusion criteria. Chemo patients did not differ significantly from No-chemo group in terms of severity of acute diverticulitis at index admission (13.2% vs. 4.4%, respectively, $p = 0.12$), resumption of chemotherapy (median 2 months), failure of non-operative management (13.2% vs 4.4%, respectively, $p = 0.12$), frequency of recurrence (20.5% vs 18.5%), hospital length of stay ($p = 0.08$), and likelihood of interval resection (24.0% vs. 16.2%, respectively, $p = 0.39$). Chemo patients recurred with more severe disease, were more likely to undergo emergent surgery (75.0% vs. 23.5%, respectively, $p = 0.03$), and were more likely to be diverted (100.0% vs. 25.0%, respectively, $p = 0.03$). Chemo patients were significantly more likely to incur a postoperative complication (100% vs 9.1% $p < 0.01$) following interval resection. Overall mortality was significantly higher in the Chemo vs. No-chemo group. Median survival in Chemo patients was 3.4 years; in No-chemo patients, median survival was not reached at 10 years.**Conclusion**: Our data do not support routine elective surgery for acute diverticulitis in patients receiving chemotherapy. Non-operative management in the acute or interval setting appears preferable whenever possible.

1. Introduction

Colonic diverticular disease affects approximately 25% of the general population, with an increased prevalence in Western and industrialized countries, and in older adults [1–6]. Approximately 15% of patients with diverticulosis will eventually develop

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diverticulitis [7,8]. Most episodes of diverticulitis involve only mild colonic inflammation that resolves with oral antimicrobial therapy and dietary modification. However, complicated diverticulitis ensues in 10% to 15% of cases, leading to perforation and abscess formation or, in severe instances, secondary fecal peritonitis, abdominal sepsis, and death [9,10]. Following an initial episode of diverticulitis managed non-operatively, recurrence rates range from 13% to 40% [11–16]. When considering an interval segmental resection, the risk of subsequent recurrence and related complications must be assessed. Recent data suggests that there is a relatively low risk of recurrence following a single episode of diverticulitis, and a low risk of emergent surgical intervention. Therefore, traditional indications for interval resection have been relaxed [12,17,18].

Traditionally, the immunosuppressed (IMS) patient has been considered at increased risk of complicated and recurrent diverticulitis. Several series report increased morbidity and mortality from acute diverticulitis in IMS patients, and a high likelihood that non-operative management (NOM) will fail [17,19,20]. As a result, some authors have argued for interval resection following an initial episode of diverticulitis in IMS patients [4,17,21,22] [23]. However, these studies are limited by small sample sizes, variable types of immunosuppression, and a lack of follow-up beyond the initial hospitalization for diverticulitis. In particular, there has been no comparison of risk or severity of recurrence in cancer patient who are on chemotherapy (Chemo) to those who are not (No-chemo). Patients with cancer have dysregulation of their immune system. When we discuss the issue of immunity in cancer patients, we should consider other contributing factors which could influence results, such as type of cancer, use of chemotherapeutic agents, stem cell transplantation, use of corticosteroids and radiation therapy. As a result, it is very difficult to differentiate between immunosuppressed and immunocompetent patients in this diverse population. Interval resection decreases the risk of recurrent diverticulitis; however, major abdominal surgery exposes patients to morbidity and potential interruption of life-prolonging chemotherapy. We studied the immediate and long-term outcomes of patients hospitalized for acute diverticulitis who were actively receiving systemic chemotherapy, in the hope that these data may help in clinical decision-making for cancer patients experiencing an episode of acute diverticulitis. Our primary aim was to assess whether recent systemic chemotherapy is associated with an increased severity in presentation of, and morbidity and mortality from, acute diverticulitis. Our secondary aim was to assess whether systemic chemotherapy is associated with a greater likelihood of, and increased severity of, recurrence [17,19,20,24].

2. Materials and methods

This was a retrospective cohort study of adult (age >18 years) patients hospitalized with an initial episode of acute colonic diverticulitis at Memorial Sloan Kettering Cancer Center (MSKCC) from 1988 to 2004. All patients with a primary episode of acute diverticulitis who were treated at MSKCC were included in the study. For the occasional patient who was taken to the operating room without prior imaging, all episodes were confirmed by imaging or operative findings. Patients were initially identified using the codes for diverticulitis (562.11 and 562.13) as specified in the International Classification for Disease, 9th and 10th revision. The diagnosis for each patient was subsequently confirmed based on computed tomography findings or operative pathology. Patients with prior episodes of diverticulitis, either at our hospital or elsewhere, were excluded from the study. The primary independent variable was recent exposure to systemic chemotherapy; patients who received systemic chemotherapy within one month of admission for diverticulitis (Chemo group) were compared to patients who had not (No-chemo group). Exposure to chemotherapy greater than one month prior to the episode of diverticulitis was considered insufficient to cause immunosuppression [25–27], and such patients were included in the No-chemo group. We selected 1 month as the cut-off, as that is typically the period during which we avoid elective cancer surgery; this is due to concerns about immunosuppression and interference with wound healing. Both the type and number of chemotherapeutic agents were abstracted, as was concurrent use of corticosteroids in both the Chemo and No-chemo groups.

Additional demographic variables included age (years), gender, and cancer diagnosis (none, lymphoma/leukemia, aerodigestive/gynecologic/genitourinary, other). Laboratory variables included admission white blood cell count (K/uL) (WBC), admission absolute neutrophil count (K/uL) (ANC), neutropenia (ANC < 1.5 K/uL), and admission serum albumin concentration (g/dL). Variables related to the index episode of acute diverticulitis included anatomic location (rectosigmoid vs. other), complicated (phlegmon, abscess, perforation, obstruction, or fistula) vs. uncomplicated, initial NOM, failure of NOM, surgical intervention at any time during the index admission, type of operation (primary anastomosis vs. diversion), hospital length of stay (LOS) (days), postoperative complications, and mortality.

Non-operative management was defined as any trial of medical management in lieu of an immediate operation for diverticulitis. Although details of NOM varied, the approach generally involved antimicrobial therapy, intravenous hydration, bowel rest, and advancement to low-residue diet following resolution of inflammatory markers (i.e., fever, leukocytosis, abdominal tenderness). Failure of NOM was defined as an operation for diverticulitis, at any time during the index admission, in a patient for whom NOM was initially attempted. Patients who failed NOM underwent open exploration. None of the patients in this series received laparoscopic wash-out. Diverticulitis was graded with the Hinchey classification for the initial as well as the recurrent episode. Postoperative complications were abstracted according to a standardized institutional complication-reporting system [28] (Table 1).

Standardized chemotherapy records were searched to obtain both the intended and actual date of the next chemotherapy, so that any interruption and resumption of treatment could be determined. Medical records were also searched until 2010 for evidence of recurrence, interval resection, or stoma reversal (where applicable). Recurrent diverticulitis was defined and characterized using

Table 1
Chemotherapeutic agents.

Chemotherapeutic agent	*n* (%)
Doxorubicin	22 (56.4)
Vinca alkaloids	15 (38.5)
Taxol	12 (30.8)
Cyclophosphamide	10 (25.6)
Platinum	10 (25.6)
5-Flourouraicil	4 (10.3)
Gemcitabine	4 (10.3)
Cytoxan	4 (10.3)
Biologics	4 (10.3)
Other	5 (12.8)
Etoposide	3 (7.7)

Percentages do not sum to 100, as 36/39 patients (92.3%) had been exposed to multiple chemotherapeutic agents at the time of index hospitalization for diverticulitis.