



## Intestinal perforation in gynecologic oncology: Do all patients benefit from surgical management?

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### HIGHLIGHTS

- Bowel injury in patients with gynecological cancers portends a poor prognosis.
- The main determinant of survival is the extent of disease at the time of perforation.
- Surgical management is unlikely to benefit patients with widely metastatic disease.

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### ABSTRACT

**Objective.** To identify those patients with gynecologic cancers and intestinal perforation in whom conservative management may be appropriate.

**Methods.** A retrospective review was performed of all gynecologic oncology patients with intestinal perforation at our institution between 1995 and 2011. The Kaplan–Meier method and Cox proportional hazards models were used to analyze factors influencing survival.

**Results.** Forty-three patients met the study criteria. The mean age was 59 years (range: 38–82 years). A large number of patients had peritoneal carcinomatosis and history of bowel obstruction. Surgery was performed in 28 patients, and 15 were managed conservatively. Overall mortality at 1, 3, 6, and 12 months was 26%, 40%, 47%, and 59%, respectively. Only cancer burden at the time of perforation was independently predictive of mortality. Patients with peritoneal carcinomatosis, distant metastasis, or both were at 42 times higher risk of death than those with no evidence of disease (95% CI: 3.28–639.83), and at 7 times higher risk of death than those with microscopic/localized disease (95% CI: 1.77–29.94). When adjusted for the extent of disease spread, management approach (conservative vs. surgical) was not a significant predictor of survival ( $p \geq 0.05$ ). The length of hospital stay (19 days vs. 7 days) and the complication rate (75% vs. 26.7%) were significantly higher in the surgical group than in the non-surgical group ( $p < 0.05$ ).

**Conclusions.** Patients who develop intestinal perforation in the setting of widely metastatic disease have a particularly poor prognosis. Aggressive surgical management is unlikely to benefit such patients and further impairs their quality of life.

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### Introduction

Patients with gynecologic malignancies are especially prone to bowel injury, which can occur in various forms. One, intestinal perforation, is generally considered an emergent condition associated with high mortality [1,2]. Any part of the gastrointestinal tract may become perforated and cause spillage of the intestinal contents into the peritoneal cavity,

leading to the development of peritonitis, intra-abdominal abscess, or both. In some instances, the perforation may be small and effectively walled off by surrounding abdominal structures, thus localizing the inflammation and infection. Although the exact cause cannot be determined for every single patient, several mechanisms explain the prevalence of bowel injuries in gynecologic cancer. First, tumor invasion of the bowel is common in advanced stage ovarian, fallopian tube, and primary peritoneal cancers. Second, radiation is frequently administered in patients with cervical cancer and can potentially cause radiation-related bowel complications. Third, intestinal perforation is a well-known complication of bevacizumab (Avastin by Genentech, San Francisco, CA, USA), a humanized monoclonal antibody against

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vascular endothelial growth factor that is increasingly being used in patients with recurrent epithelial ovarian cancer.

Immediate surgery is often necessary in the event of bowel injury except when the leak is walled off; in these cases conservative treatment with careful observation may be justified. However, patients with gynecologic cancers are often of advanced age and frequently have concurrent co-morbidities. In addition, the life expectancy of some may already be limited due to an extensive cancer burden that has been treated with multiple chemotherapy regimens. A few studies, including one from our own institution, have evaluated the outcomes in gynecologic oncology patients diagnosed with bowel injury [3–5]. The previous studies have suggested that prognosis is poor in such patients and that management approaches should be carefully considered. This current study specifically identifies those patients with gynecologic cancers in whom an aggressive surgical management of bowel injury may be counterproductive, and thus provides important information to aid decision-making in these difficult clinical situations.

## Methods

After obtaining approval from the Institutional Review Board, a retrospective chart review was performed for all patients treated at our institution for gynecologic cancer and intestinal perforation between January 1, 1995 and December 31, 2011. ICD-9 codes were used to identify the study subjects. The following data were abstracted from the patients' charts: demographic information, medical co-morbidities, cancer type and treatment history, date of last contact, and vital status at last follow-up. The details regarding the bowel injury, including presenting symptoms, laboratory values, management, and outcome of the patients, were also recorded. Patients were divided into three groups based on the disease status at the time of perforation as determined by the findings recorded in the CT scan and/or operative reports. Patients with no evidence of disease were placed in one group, those with microscopic disease or localized disease (e.g., an isolated pelvic mass) were in the second group, and patients with peritoneal carcinomatosis, distant metastasis, or both constituted the third group. Bowel injury was diagnosed by either free air on abdominal radiograph or CT scan, evidence of contrast extravasation on a CT scan, or presence of bowel contents in the abdomen on surgical exploration. Patients who underwent a surgical treatment for their cancer were considered to have undergone a cancer-directed surgery. Information on use of radiation and chemotherapy was also collected and included administration of these therapies at any time during the cancer treatment. We also included in our analyses a modified version of the Charlson comorbidity index, which was based on the ten conditions captured from the past medical history of all patients [6].

Statistical analyses were performed by using SAS 9.2 (SAS Institutes, Cary, NC). Simple descriptive statistics were used to describe the study cohort. The Student's *t*-test was used for the continuous variables, and the Fisher's exact test was used for categorical variables. Survival time was defined from the date of diagnosis of intestinal perforation to the date of last contact or date of death. The Kaplan–Meier method with log-rank and Wilcoxon tests was used for univariate analysis of differences between the groups. Cox proportional hazards regression models were used for multivariate analysis. All *p*-values reported are two-tailed, and a *p*-value of less than 0.05 was considered to be statistically significant.

## Results

The study group comprised 43 patients. The mean age was 59.4 years (range: 38–82 years). The demographic and clinical characteristics of the cohort are shown in Table 1. Most patients were white and had a BMI of less than 30. The Charlson co-morbidity index score was 0 in 63% of the patients. The patient population was fairly evenly distributed across different time periods (1995–2000, 2001–2006, and

**Table 1**  
Patient and disease characteristics.

Variable	Number (%)
Mean age at diagnosis (range)	59.4 years (38–82 years)
Race	White 35 (81.4%) Black 8 (18.6%)
BMI	<30 32 (74.4%) ≥30 11 (25.6%)
Charlson co-morbidity index	0 27 (62.8%) ≥1 16 (37.2%)
Year of diagnosis	1995–2000 11 (25.6%) 2001–2006 17 (39.5%) 2007–2011 15 (34.9%)
Cancer type	Uterine 13 (30.2%) Cervix 11 (25.6%) Ovarian/fallopian tube/primary peritoneal 17 (39.5%)
Stage	Vulva/vagina 2 (4.7%) I/II 16 (37.2%) III/IV 21 (48.8%) Unknown 6 (14.0%)
Cancer-directed surgery	Yes 31 (72.1%) No 11 (25.6%) Unknown 1 (2.3%)
Radiation	Yes 21 (48.8%) No 20 (46.5%) Unknown 2 (4.7%)
Chemotherapy	Yes 34 (79.1%) No 6 (14.0%) Unknown 3 (6.9%)
Chemotherapy Regimen	<2 17 (50.0%) ≥2 14 (41.2%) Unknown 3 (8.8%)
Site of perforation	Small bowel 21 (48.8%) <sup>a</sup> large bowel 10 (23.3%) <sup>a</sup> Sigmoid colon 9 (20.9%) Stomach 1 (2.3%) Unknown 4 (9.3%)
Extent of cancer present at the time of perforation	No evidence of disease 8 (18.6%) Microscopic disease/localized disease 10 (23.3%) Peritoneal carcinomatosis/distant metastasis 22 (51.1%) Unknown 3 (7.0%)
Ca-125	<100 10 (23.3%) ≥100 16 (37.2%) Unknown 17 (39.5%)
Prior or concurrent bowel obstruction	Yes 24 (55.8%) No 17 (39.5%) Unknown 2 (4.7%)
Management of perforation	Conservative 15 (34.9%) Surgical 28 (65.1%)

<sup>a</sup> Perforation was present in small- and large bowel in 2 patients.

2007–2011). Ovarian/fallopian tube/primary peritoneal cancers were more common than cancers originating in other parts of the female genital tract. Cancer-directed surgery was performed in 72% of the patients, 49% received radiation treatment, and chemotherapy was administered in about 79% of the patients. A total of 40% of the cohort was treated with both chemotherapy and radiation (either concurrently or at different time points). Most patients had received only one prior regimen at the time of perforation, with platinum/taxane being the most commonly used combination. Although most perforations occurred in the small bowel (49%), the sigmoid colon was involved in 21% of the patients. A large number of the patients (51%) had widespread disease as determined by the presence of peritoneal carcinomatosis, distant metastasis, or both at the time of perforation. Bowel obstruction, either prior or concurrent, was noted in about 56% of the patients. The treatment for perforation was surgical in 65% of the patients and conservative in the remaining 35%. Of the 28 patients who underwent surgery, 4 had failed an initial attempt at conservative management. Surgical procedures performed were abdominal exploration and bowel resection in 19 patients, ileostomy in four patients, colostomy in four patients, and

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