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Management of Bowel Obstruction in Patients with Advanced Ovarian Cancer

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In a retrospective study, 58 patients with bowel obstruction due to advanced ovarian cancer were analysed. In a forward stepwise proportional hazard regression analysis, we looked for factors influencing bowel obstruction-free survival. Patients who presented with bowel obstruction as the first sign of ovarian cancer and those with a longer interval between last cancer treatment and bowel obstruction did better. Patients with ascites did worse. No other independent factors were found. Based on these data, we classified patients into a favourable prognosis group (no previous treatment or interval since last treatment exceeding 6 months; no ascites) and a poor prognosis group (interval since last treatment shorter than 6 months; ascites). Patients from the favourable prognosis group had a median bowel obstruction-free survival of 8 months, compared to 1 month for the poor prognosis group ($P < 0.001$). Surgery had a marginally significant positive effect on bowel obstruction-free survival when compared to medical treatment in the favourable prognosis group ($P = 0.052$). Surgery had no effect at all in the poor prognosis patients.

Key words: bowel obstruction, ovarian cancer, surgery
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INTRODUCTION

OVARIAN CANCER is still a devastating disease and is responsible for approximately 6% of all cancer deaths in the western world [1–3]. The disease remains the leading cause of gynaecological cancer mortality. Approximately 75–80% of patients present with advanced stage III and stage IV disease, where prognosis is poor despite intensive treatment. Transperitoneal dissemination is the most commonly observed mode of spread of ovarian cancer. The main treatment modality for advanced disease is cytoreductive surgery, followed by combination chemotherapy, using platinum-based regimens.

Cancer-related bowel obstruction is a common problem in patients with advanced disease [1, 4–6]. Usually, patients with obstruction are initially treated by medical means: nasogastric

suction and intravenous (i.v.) fluids. If decompression does not adequately relieve symptoms, or if they recur on resumption of oral intake, palliative surgery should be considered. The dilemma of whether or not to operate is a difficult one, as some patients obviously benefit from surgery and others die in the early postoperative period, and the additional pain and discomfort of a laparotomy can hardly be called palliation [7–9].

The Netherlands Cancer Institute has a strong tradition in second-line management and research in ovarian cancer patients, and consequently, its clinicians are frequently confronted with the decision of surgical relief of bowel obstruction. The aim of this study is to describe our experience, and to identify prognostic indicators for successful intervention.

PATIENTS AND METHODS

From the registry of the Netherlands Cancer Institute, the records of all patients having advanced ovarian cancer and who were treated for bowel obstruction were retrieved. In the period 1984–1991, 60 patients were found, of whom 2 were excluded because of insufficient data, leaving 58 cases for analysis. From the records, data were collected concerning diagnosis and treatment (of the ovarian cancer), clinical parameters at the moment of bowel obstruction, information on the treatment of bowel obstruction, the results of that treatment and the final outcome.

Statistical methods

For statistical analysis, the outcome was considered to be successful as long as the patients were alive and without recurrent bowel obstruction (bowel obstruction-free survival). A failure was defined as death of the patient or recurrent bowel obstruction.

Bowel obstruction-free survival curves were calculated using the Kaplan–Meier method. A forward stepwise proportional hazard (Cox) regression analysis was used to identify potentially prognostic factors, and to test the difference between medical and surgical treatment of bowel obstruction, controlled for those factors. Criterion to enter (or remove) a variable was P value < 0.05 (> 0.05).

In testing a particular variable, patients were counted as missing if no information was available for that variable, or for variables already controlled for. Ordinal and interval variables were used linearly, but linearity was tested for, comparing the log-likelihoods of the models with and without dummy variables for certain categories, in addition to the linear term.

Patients' characteristics

Mean age was 55.25 years (range 34–75.5) at the time of first diagnosis of ovarian cancer.

The FIGO stage at first diagnosis was recorded: stage I 3 cases, stage II 3 cases, stage III 41 cases, stage IV 5 cases, not recorded 6 cases. Primary cytoreductive surgery was performed in 51 patients. In addition, 8 patients were treated by radiotherapy. All patients underwent chemotherapeutic treatment, either as part of their primary treatment or because of recurrent disease. Patients received an average of 5.1 courses of chemotherapy; 32 received more than six courses. A variety or regimens were used during this period, all containing cisplatin or carboplatin. The diagnosis of recurrent ovarian cancer was established by gynaecological pelvic examination, computer tomography (CT) scan and a significant rise in serum CA 125 levels.

Mean time between first diagnosis of ovarian cancer and the diagnosis of bowel obstruction was 19.0 months (range 0–116). Mean time between bowel obstruction and last cancer therapy was 6.2 months (range 0–41). Bowel obstruction was the first sign of advanced ovarian cancer in 8 patients.

The diagnosis of bowel obstruction was made on physical examination, and on the presence of bowel dilatation on plain abdominal X-ray. In 29 patients, distension was predominantly of the small bowel, in 17 cases the large bowel was mainly affected, in 5 patients both were affected, and in 7 patients the files were not clear in this respect. At the time of bowel obstruction, serum albumin measurements were < 35 g/l in 12/39 cases for whom this parameter was recorded. CA 125 test levels were recorded in 41 patients: in 11 cases this was > 2000 U/l, in 14 cases 200–2000 U/l and in 16 cases < 200 U/l. Ascites were detected in 24 patients, either on sonography or at operation, 18 patients had no ascites and the information was not available for 16 patients. The number of previous operations before the current intervention was registered. Patients on average underwent 2.8 previous operations (range 1–7).

Bowel obstruction was initially medically treated in all patients, i.e. nasogastric suction, i.v. infusion and analgesics. In 30 patients, the decision was made to perform a laparotomy. All patients were followed until the time of death or recurrent bowel obstruction.

RESULTS

Surgery was not performed in 28 of the 58 patients. 12 patients improved sufficiently to resume oral nutrition. 16 patients did not improve, but were judged unsuitable for surgery and subsequently died. Criteria for this decision were not clearly recorded.

Of the 30 patients who underwent laparotomy, the intervention consisted of adhaesiolysis in 5 cases, small bowel resection or by-pass in 16 cases, ileostomy in 10 cases and colostomy in 9 cases. Sometimes more than one procedure was carried out. In the statistical analysis, no attempt was made to subdivide the surgery group according to type of intervention.

3 patients died within 15 days of the operation, and an additional 7 patients died within 45 days, mostly of persistent bowel obstruction. In 18 patients full oral intake was restored: 8 were patients who presented with bowel obstruction as first sign of their ovarian cancer, and 10 were patients who had already had extensive chemotherapy. 2 patients lived longer than 45 days, but had to be kept on intravenous nutrition.

Median bowel obstruction-free survival for all patients was 2 months. Table 1 shows the results of the stepwise analysis for bowel obstruction-free survival. Step 0 is equivalent to univariant analysis. Here, the most important prognostic factor appears to be the time from last cancer treatment to bowel obstruction, acting in a non-linear way: a relatively favourable prognosis for patients with either no previous treatment for ovarian cancer (interval 0) or an interval of 10 months or more. In a more refined analysis the differences appeared to be between the categories 0, 1–5 and > 6 months ($P = 0.0036$). This partition was used in subsequent steps to control the effect of other variables for the interval from last treatment to bowel obstruction. Also univariantly, surgically treated patients appeared to have a better bowel obstruction-free survival than

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Table 1. Forward stepwise proportional hazard (Cox) regression analysis for potential prognostic factors of bowel obstruction-free survival

Variable	*P* values Step 0	Step 1	Step 2
Stage	NS	NS	NS
Previous surgery	NS	NS	NS
Type of primary surgery	NS	NS	NS
No. of laparotomies	NS	NS	NS
Total number of operations (non-linear)	NS	NS	NS
Type of primary chemotherapy	NS	NS	NS
No. of courses chemotherapy (non-linear)	NS	NS	NS
Response to primary chemotherapy (non-linear)	NS	NS	NS
Primary radiotherapy	NS	NS	NS
Interval diagnosis-bowel obstruction (non-linear)	NS	NS	NS
Interval last treatment—bowel obstruction (non-linear); includes interval 0)	0.0036* (0.0021)	0.0036* (0.0021)	0.0001* (0.00)
Age at bowel obstruction (non-linear)	NS	NS	NS
Type of bowel obstruction	NS	NS	NS
Ascites	NS	0.0020	NS
Albumin (non-linear)	NS	NS	0.0020
CA125 (non-linear)	NS	NS	NS
Treatment bowel obstruction	0.024	NS	NS

NS, non-significant. In parentheses, the *P* values for linearity.
* *P* value including non-linearity. Step 0 equals univariant analysis. In step 1 calculations were made controlling for interval last cancer treatment to bowel obstruction. In step 2 calculations were made controlling both for interval last cancer treatment to bowel obstruction and for ascites.

medically treated patients. The bowel obstruction-free survival for conservatively treated patients was 1 month compared with 4 months for surgically treated patients ($P = 0.024$).

Controlling for the interval from last cancer treatment to bowel obstruction (step 1), the significance of the difference between the treatment groups disappeared, although the presence of ascites appeared to be an additional unfavourable characteristic. Univariantly, this was masked because, in patients with ascites, the otherwise most favourable group without previous treatment (interval 0) appeared to be overrepresented.

Controlling for both the interval from last cancer treatment to bowel obstruction and the presence of ascites, no other variables attained a P value < 0.05.

Bowel obstruction-free survival curves, depending on combinations of ascites status and interval between bowel obstruction and last cancer treatment were constructed. Based on these graphs, two prognostic groups could be defined: (i) patients with favourable prognosis: no previous treatment (with or without ascites), or interval from last cancer treatment to bowel obstruction > 6 months, without ascites; (ii) patients with poor prognosis: interval from last cancer treatment to bowel obstruction of 1–5 months (with or without ascites), or interval > 6 months but with ascites.

Bowel obstruction-free survival curves for these two groups are demonstrated in Figure 1. Median bowel obstruction-free survival for the patients with favourable prognosis was 8 months

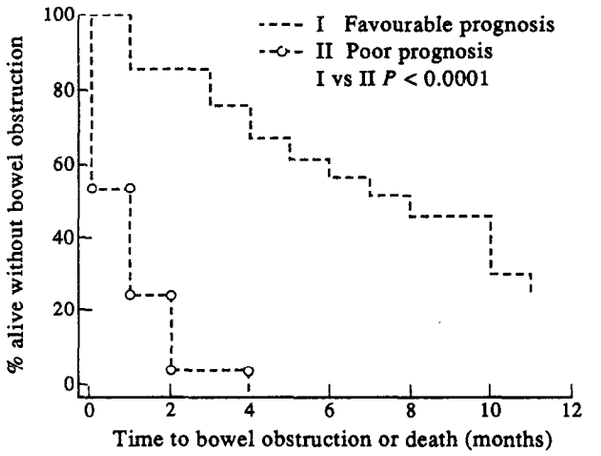

Figure 1. Bowel obstruction-free survival, by prognostic groups. I: Favourable prognosis group, consists of patients who either presented with bowel obstruction as the first sign of ovarian cancer, or had an interval between last cancer treatment and bowel obstruction exceeding 6 months and did not have ascites. II: Poor prognosis group includes patients who had a short interval (1–5 months) between last cancer treatment and bowel obstruction, or had a longer interval, but with ascites.

and for patients with poor prognosis 1 month. At 6 months, 56% of patients with favourable prognosis but no patients with poor prognosis were still alive without bowel obstruction.

Figure 2 shows bowel obstruction-free survival curves for patients with favourable and poor prognosis in relation to the type of treatment they received: medical or surgical. For patients with favourable prognosis, surgical treatment of their bowel obstruction appeared to improve bowel obstruction-free survival, although the difference did not reach statistical significance ($P = 0.052$). Surgical treatment did not influence the bowel obstruction-free survival in patients in the poor prognosis group.

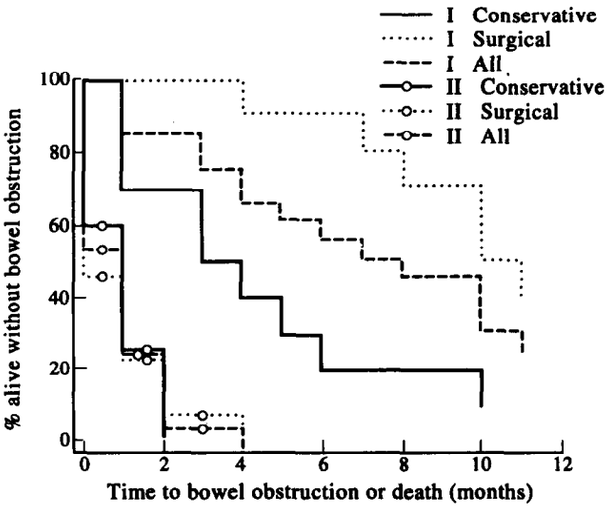

Figure 2. Bowel obstruction-free survival in relation to prognostic groups and therapy. I: Favourable prognosis group. II: Poor prognosis group. Surgery versus conservative treatment, within favourable prognosis group I: $P = 0.052$. Surgery versus conservative treatment within poor prognosis group: NS.

DISCUSSION

In the Netherlands Cancer Institute, as in most centres, the initial care for patients with advanced ovarian cancer and bowel obstruction has been medical, by means of nasogastric suction and intravenous infusion. The management is carried out with the close cooperation of surgeons, gynaecologists and medical oncologists. Together they face the decision of whether to perform surgery, if obstruction does not resolve under this regimen. In the period that is covered by this study, we did not systematically use a set of criteria to direct that decision. However, the decision to perform a laparotomy was clearly not a random one, but was influenced by factors such as the performance state of the patient, the chances of response to (further) chemotherapy, and the patient's motivation to continue. In this way, an important selection bias was introduced favouring patients treated by operation. To overcome this bias, we used a forward stepwise proportional hazard (Cox) analysis, in which type of treatment was entered as one of many factors that might influence the outcome. Not surprisingly, surgically treated patients did better than medically treated patients in step 0 (univariantly), but in multivariant analysis, type of treatment was no longer a significant factor. In this multivariant analysis, the interval between previous cancer treatment and bowel obstruction, and the presence of ascites remained as the only independent factors significantly influencing bowel obstruction-free survival.

Based on these data, we classified patients into two groups: a group with a relatively favourable prognosis (I) and one with a poor prognosis (II). The favourable prognosis group consists of patients who either presented with bowel obstruction as the first sign of ovarian cancer, irrespective of the presence of ascites, or had an interval between last cancer therapy and bowel obstruction exceeding 6 months, and did not have ascites. The poor prognosis group consisted of patients who had an interval between last cancer treatment and bowel obstruciton of less than 6 months, or had a longer interval but with ascites. The difference in bowel obstruction-free survival between these groups was highly significant ($P < 0.0001$), with a median of 8 months for the favourable prognosis group and only 1 month for the poor prognosis group. Even more important is the finding that surgery had a positive effect on bowel obstruction-free survival in patients from the favourable prognosis group ($P = 0.052$). In patients from the poor prognosis group, surgery did not change the poor outcome at all, notwithstanding the selection bias in favour of operated patients.

Based on these findings, we conclude that this simple classification gives relevant information to the clinician who has to decide about surgery in patients with bowel obstruction in advanced ovarian cancer. Krebs [8] propagated, in 1983, a prognostic index with the same aim, based on age, nutritional status, previous radiotherapy, previous chemotherapy and presence of ascites. Larson and colleagues confirmed the value of this index [10]. Others, however, did not find the prognostic value of some, or all of the factors included in the Krebs index [4, 11, 12]. Age and nutritional status had no prognostic significance in our data.

The differences between our favourable and poor prognosis groups appear understandable to us. Patients who present with bowel obstruction as the first sign of ovarian cancer do better because most of them will respond to platinum-based chemotherapy in the first line. However, at present, almost all patients have been extensively treated by platinum-based chemotherapy before they develop bowel obstruction. In these patients, further chemotherapy will have less impact, and differences in prognosis depend on differences in tumour biology. Ovarian cancers that grow relatively slowly (long interval) and have a solid growth pattern, usually in the pelvis (mostly without ascites), have a relatively favourable prognosis. In that situation surgical intervention has a chance. If, however, the tumour is growing fast (short interval) and is diffuse (ascites), the prognosis is poor, and surgery is unlikely to be of any palliative value. This might alter when better second-line chemotherapy becomes available for these patients.

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