Published in final edited form as:

Gynecol Oncol. 2012 June ; 125(3): 614–620. doi:10.1016/j.ygyno.2012.02.027.

Incidence of and risk factors for postoperative ileus in women undergoing primary staging and debulking for epithelial ovarian carcinoma[☆]

Jamie N. Bakkum-Gamez^{a,*}, Carrie L. Langstraat^a, Janice R. Martin^b, Maureen A. Lemens^b, Amy L. Weaver^c, Sumer Allensworth^a, Sean C. Dowdy^a, William A. Cliby^a, Bobbie S. Gostout^a, and Karl C. Podratz^a

^a Division of Gynecologic Surgery, Mayo Clinic, Rochester, MN, USA

^b Surgery Research, Mayo Clinic, Rochester, MN, USA

^c Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA

Abstract

Objective—Thorough primary cytoreduction for epithelial ovarian carcinoma (EOC) improves survival. The incidence of postoperative ileus (POI) in these patients may be underreported because of varying POI definitions and the evolving, increasingly complex contemporary surgical approach to EOC. We sought to determine the current incidence of POI and its risk factors in women undergoing debulking and staging for EOC.

Methods—We retrospectively identified the records of women who underwent primary staging and cytoreduction for EOC between 2003 and 2008. POI was defined as a surgeon's diagnosis of POI, return to nothing-by-mouth status, or reinsertion of a nasogastric tube. Perioperative patient characteristics and process-of-care variables were analyzed. Univariate analyses were used to identify POI risk factors; variables with $P \leq .20$ were included in multivariate analysis.

Results—Among 587 women identified, the overall incidence of POI was 30.3% (25.9% without bowel resection, 38.5% with bowel resection; $P = .002$). Preoperative thrombocytosis, involvement of bowel mesentery with carcinoma, and perioperative red blood cell transfusion were independently associated with increased POI. Postoperative ibuprofen use was associated with decreased POI risk. Women with POI had a longer length of stay (median, 11 vs 6 days) and increased time to recovery of the upper (7.5 vs 4 days) and lower (4 vs 3 days) gastrointestinal tract ($P < .001$ for each).

Conclusions—The rate of POI is substantial among women undergoing staging and cytoreduction for EOC and is associated with increased length of stay. Modifiable risk factors may include transfusion and postoperative ibuprofen use. Alternative interventions to decrease POI are needed.

Keywords

Bowel recovery; Ovarian cancer; Postoperative ileus

[☆]Presented at the annual meeting of the American College of Surgeons, San Francisco, California, October 23–27, 2011.

© 2012 Elsevier Inc. All rights reserved.

* Corresponding author at: Division of Gynecologic Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA. Fax: +1 507 266 9300. bakkum.jamie@mayo.edu (J.N. Bakkum-Gamez).

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Introduction

In 2010, an estimated 21,880 women in the United States had a new diagnosis of epithelial ovarian cancer (EOC), and an estimated 13,850 women died of the disease [1]. Approximately 75% of women with EOC will have advanced-stage disease (International Federation of Gynecology and Obstetrics [FIGO] stages III and IV), characterized most often by widely disseminated abdominal and pelvic tumor implants [2]. Increasing evidence shows that complete cytoreduction to microscopic residual disease followed by systemic adjuvant platinum- and taxane-based chemotherapy yields superior survival [2–6]. Depending on individual extent and pattern of disease spread, surgical cytoreduction often consists of an extensive abdominopelvic operation that may include peritonectomy, splenectomy, diaphragm stripping or resection, and large and/or small bowel resection (BR) [2,7–9]. Carcinomas of the ovary, fallopian tube, and peritoneum are managed similarly [5,10–12].

In more than 90% of women who require BR during primary surgery for EOC, the indication for BR is cytoreduction [3]. Studies assessing complications after large BR in women undergoing EOC cytoreduction often focus on the risk of bowel leak (reported range, 2.0%–8.7%) [9,13,14]. However, the rate of postoperative ileus (POI) after large BR, or a combination of large and small BR, performed during EOC debulking appears higher than the rate of bowel leak, with previously reported rates of POI ranging from 7.6% to 30.0% [3,14,15]. These rates reflect the incidence of POI from 1 to 3 decades ago. Further, given increasing evidence that maximal surgical effort with cytoreduction to microscopic residual disease provides a survival advantage [4,8,16,17], surgical complexity has undoubtedly increased and the contemporary rate of POI may indeed be even higher.

Large bowel function returns approximately 72 h after laparotomy [18,19]; retroperitoneal dissection, which is required for pelvic and para-aortic lymphadenectomy, increases colonic stasis and POI [19,20]. Delays in gastrointestinal tract (GI) recovery increase hospitalization duration by approximately 30% and increase care costs in excess of \$5000 to \$10,000 per ileus [21]. In the current economic climate, judicious, cost-effective postoperative care is a priority. GI recovery is a key driver in determining postoperative hospital discharge readiness, and costs associated with delayed GI recovery are substantial [21–23]. Mean total hospitalization cost for patients undergoing colectomy was \$8182 more in patients with POI than in those without POI in a large national inpatient database [21]. In a single-institution study, costs for patients undergoing simple hysterectomy or hemicolectomy who had POI were \$4512 and \$12,416 more, respectively, than for patients without POI [24]. Moreover, among women with advanced-stage EOC undergoing rectosigmoid resections, the incidence of prolonged POI requiring nutritional support with total parenteral nutrition is approximately 6% [9]. As costs continue to increase, novel methods to decrease POI and length of stay (LOS) are needed to improve patient care and the cost-effectiveness of postoperative management in women undergoing cytoreduction for EOC.

Uncomplicated GI recovery is also associated with improved non-GI postoperative outcomes. Among patients undergoing BR, the introduction of fast-track and enhanced recovery postoperative pathways has demonstrated significant decreases in postoperative LOS and overall surgical complications [25–27]. Early feeding after colorectal surgery has been shown to decrease wound infection rates, decrease pneumonia, and improve anastomotic healing [28]. Early efforts in EOC have reported similar effects of fast-track postoperative care in decreasing LOS and postoperative complications. However, few data are available in the literature on GI recovery after surgery for EOC, regardless of fast-track use, compared with that for colorectal disease [29,30]. The disease spread patterns for the 2

cancers are quite different—EOC is diffuse whereas resectable colorectal cancers are more focal—and the surgical complexity of EOC staging and cytoreduction has evolved markedly in recent years. For these reasons we sought to investigate the incidence of and risk factors for POI in the contemporary surgical care setting for the primary surgical staging and debulking of EOC, fallopian tube cancer (FTC), and primary peritoneal cancer (PPC).

Methods

Patient population

We retrospectively searched our patient database for the records of women with primary EOC, FTC, and PPC who underwent primary surgical staging and cytoreduction at Mayo Clinic, Rochester, Minnesota, from January 1, 2003, to December 29, 2008. Patients were excluded if they underwent prior surgical diagnosis of their current cancer via laparoscopy or laparotomy, received neoadjuvant chemotherapy, were undergoing surgery for recurrent disease, had a nonepithelial malignancy, or had denied access to their medical records for research purposes. Mayo Clinic Institutional Review Board approval was obtained for the study.

Data collection

Objective perioperative data and subjective patient-provided GI function data were obtained from the medical record by a trained, dedicated registered nurse data abstractor. The American College of Surgeons' National Surgical Quality Improvement Program platform, which contains more than 130 elements for analyzing patient risk factors and process-of-care variables, was used [31,32]. Factors that might influence POI, such as patient risk factors (e.g., age, body mass index [BMI], performance status, comorbid conditions), process-of-care variables (e.g., surgical complexity, operating time, estimated blood loss), disease-specific parameters (e.g., stage, grade, histologic type), analgesics used perioperatively (e.g., narcotics, nonsteroidal anti-inflammatory drugs), and postoperative complications (e.g., POI, bowel leaks, readmission within 30 days of surgery) were abstracted from patient charts. Variables used to characterize postoperative bowel function included the number of days to first general diet intake, days to first postoperative flatus, days to first postoperative bowel movement, and days to dismissal. Also collected were the occurrence of postoperative emeses, need for postoperative reinsertion of a nasogastric tube, and the need for postoperative in-hospital imaging.

POI was defined as any 1 or more of the following occurrences within 30 days of initial surgery: 1) surgeon diagnosis of POI; 2) return to nothing-by-mouth status because of GI dysfunction; or 3) re-placement of a nasogastric tube because of GI dysfunction. All surgical procedures performed in the process of staging and debulking were recorded, and surgical complexity scores were assigned on the basis of an established calculation protocol (Box 1) [2]. All potential risk factors and disease-specific parameters with a prevalence of 5% or greater or deemed to be clinically relevant were assessed for their influence on POI.

Analgesics

All perioperative analgesics used were recorded. All intravenous narcotics were converted to morphine sulfate equivalents (MSE; in mg) [33]. Patients were assigned to quintiles of perioperative ibuprofen use (none, 600–1800, 2400–3000, 3600–4800, and >4800 mg) on the basis of total ibuprofen intake during the hospitalization, and ibuprofen quintile was correlated with average daily narcotic use (in MSE).

Statistical analyses

The statistical analysis was performed using SAS software version 9.2 (SAS Institute, Inc, Cary, North Carolina). Patient characteristics, process-of-care variables, disease-specific parameters, postoperative analgesics used, and postoperative complications were summarized using standard descriptive statistics. Univariate analyses were performed using the χ^2 test for categorical variables and the 2-sample t test or Wilcoxon rank sum test for continuous variables. BMI, platelet count, and CA-125 level were each transformed using natural logarithmic transformation before considering them in the model building. All variables with P .20 from the univariate analysis or that were considered clinically relevant were considered for entry into the multivariate logistic regression model. Both stepwise and backward variable selection methods were investigated, and variables were included in the final model if $P < .05$. The estimated parameter coefficients and their standard errors for the variables in the multivariate model were used to calculate odds ratios and corresponding 95% CIs.

Results

Patient demographics and baseline characteristics

A total of 587 cases met the inclusion criteria (Table 1). Primary EOC was the most common diagnosis (434 patients, 73.9%); 118 patients (20.1%) had PPC and 35 (6%) had FTC. The mean age at surgical diagnosis was 63.8 years (range, 33.3–90.7 years), 535 patients (91.1%) had an Eastern Cooperative Oncology Group performance status of 0 or 1, and 312 (53.2%) had an American Society of Anesthesiologists score of 1 or 2. Previous hysterectomy remote from EOC, PPC, or FTC diagnosis had been performed in 138 cases (23.5%).

Operative findings and intraoperative process-of-care variables

Most patients had extensive pelvic and upper abdominal disease at the time of initial exploration (Table 2). Advanced FIGO stage was most common; 458 patients (78.0%) were stage IIIA or higher: 3 IIIA (0.5% overall), 24 IIIB (4.1%), 325 IIIC (55.4%), and 106 IV (18.1%). Despite extensive disease, 316 patients (53.8%) underwent cytoreduction down to microscopic residual disease, and 184 (31.4%) underwent cytoreduction to less than 1 cm of residual disease. Serous histology was most common.

BR was performed in 205 patients (34.9%); 58 underwent more than 1 BR. The most common BR was a low anterior resection with reanastomosis (160, 27.3% overall), followed by other large BRs (63, 10.7%) and small BRs (50, 8.5%). Surgical complexity was classified as high for 136 patients (23.2%) and intermediate for 347 (59.1%) patients. Perioperative red blood cell transfusions were given to 452 (77%) of the patients. There was no association between BMI and surgical complexity: mean BMI was 29.2, 27.9, and 27.9 kg/m², respectively, for low, intermediate, and high complexity cases.

Perioperative bowel preparation and oral intake management

During the time period studied, the standard practice among Mayo Clinic gynecologic oncology surgeons was for patients undergoing a potential EOC staging or debulking to receive preoperative mechanical bowel preparation. Additionally, it was standard practice for an NGT to be placed at the time of surgery. Of the 587 patients included in this study, 555 (94.5%) had an NGT placed. For the 555 who had an NGT placed at the time of surgery, the median (IQR) time to removal was 1.5 days (IQR, 1.0–3.0 days), with 133 (24.0%) removed at 0.5 days, 67 (12.1%) removed at 1 day, and 111 (20.0%) removed at 1.5 days. Surgeon preference dictated the timing of NGT removal. Standard practice during this

period was to start patients on a clear liquid diet after NGT removal and to advance their diet as tolerated. The median (IQR) time to general diet was 5.0 days (IQR, 3.5–7.0) days, with a range of 0.5 to 33 days.

Perioperative analgesics

Patients received a mean of 19.8 mg MSE of intravenous narcotics per day. Most patients (348, 59.3%) received postoperative ibuprofen (Table 2); 84 patients (14.3%) received more than 4800 mg during their hospitalization.

Univariate analysis of factors associated with POI

Of the 587 patients, 178 (30.3%) had POI. Seventy-nine of the 205 women who required BR (38.5%) had POI, vs 99 (25.9%) of the 382 who did not require BR ($P=.002$). By univariate analysis, those with POI were older, had higher CA-125 level, and had more frequent pre-operative thrombocytosis (platelets $>400 \times 10^9/L$) (Table 3). Other factors significantly associated with POI included ascites, extensive initial abdominal and pelvic involvement with carcinoma, advanced FIGO stage, positive pelvic or para-aortic lymph nodes, and measurable residual disease after cytoreduction. Additionally, a higher proportion of patients with POI had undergone previous hysterectomy compared with patients without POI. Surgical complexity also significantly affected POI: POI developed in 55 of 136 patients with high-complexity surgery (40.4%), vs 93 of 347 (26.8%) with intermediate-complexity surgery, and 30 of 104 (28.8%) with low-complexity surgery. The rate of perioperative red blood cell transfusion was also significantly higher among patients with POI.

The rate of any postoperative use of ibuprofen was significantly lower among patients with POI than in those without POI. There was no trend in POI rates by quartiles of daily postoperative intravenous narcotics use: 30.3%, 29.5%, 27.4%, and 34.5%, respectively, for patients with <7.33 , 7.33–12.58, 12.59–23.88, and >23.88 MSE mg/d ($P=.55$). The median total daily postoperative intravenous narcotic dose also was not significantly different across the quintiles of total ibuprofen use during hospitalization ($P=.34$).

Postoperatively, 31 patients (5.3%) had a bowel leak or intra-abdominal abscess within 30 days of surgery. The rate of POI was higher among those with a bowel leak or abscess (21/31, 67.7%) than among those without a bowel leak or abscess (157/556, 28.2%) ($P<.001$).

Red blood cell transfusion and POI

Among the entire cohort, 452 patients (77.0%) had at least 1 peri-operative unit of red blood cells transfused: 146 received blood only intraoperatively, 99 received blood only postoperatively, and 207 received both intraoperative and postoperative transfusions. Among these 3 transfusion cohorts, the rate of POI increased significantly with increasing number of transfused units ($P=.02$, $P<.001$, and $P<.001$, respectively) (Fig. 1).

Multivariate analysis of factors associated with POI

In multivariate analyses, postoperative ibuprofen use remained associated with decreased POI risk (Table 4). Preoperative thrombocytosis, carcinoma involvement of the bowel mesentery on initial exploration, and perioperative red blood cell transfusion also remained associated with increased POI risk. There was a potential interaction in the model between postoperative ibuprofen use and preoperative platelet count greater than $400 \times 10^9/L$ ($P=.008$ in the full multivariate model). Among patients with a preoperative platelet count greater than $400 \times 10^9/L$, the odds ratio for the association between postoperative ibuprofen and POI was 0.22 (95% CI, 0.12–0.41), whereas the odds ratio for the association between

postoperative ibuprofen and POI was 0.57 (95% CI, 0.35–0.89) for patients with preoperative platelet counts of $400 \times 10^9/L$ or less.

Return of GI function and LOS

Overall median times to upper GI recovery (tolerating a general diet) and lower GI recovery (passing of flatus) were 5 days and 3.5 days, respectively. Median overall LOS was 7 days. Patients with POI tolerated a general diet later than patients without POI (median, 7.5 vs 4 days; $P < .001$). Similarly, patients with POI had first flatus later than patients without POI (median, 4 vs 3 days; $P < .001$). Median LOS was longer in patients with POI than in those without POI (median, 11 vs 6 days; $P < .001$).

Discussion

Primary surgical cytoreduction improves progression-free survival and overall survival in patients with EOC [2,4,8,10]. The complexity of most EOC surgical staging and cytoreduction surpasses that of other major abdominal surgeries, including simple hysterectomy and colorectal surgery. Even in early-stage disease, comprehensive staging (bilateral salpingo-oophorectomy, hysterectomy if uterus present, bilateral pelvic and para-aortic lymphadenectomy, and omentectomy) reaches an intermediate level of surgical complexity [2]. Increasing complexity of cytoreductive surgery has also been associated with improved overall survival independent of patient age and American Society of Anesthesiologists score [2].

The benefits of aggressive surgery, however, do not come without potential complications. The contemporary rate of POI associated with primary surgical staging and cytoreduction is substantial and higher than historically documented. Although the proportion of women who underwent BR and experienced POI in this study was high (38.5%), women undergoing staging and cytoreduction without BR were also at substantial risk for POI (25.9%), suggesting that even the minimum procedures required for comprehensive staging carry a considerable risk of POI. Interestingly, even among patients with a low surgical complexity score (≤ 3) the rate of POI was nearly 30%. It is important to note that although the rate of secondary POI among patients with a bowel leak or intra-abdominal abscess was more than 67%, those with a bowel leak or abscess represented only 5% of the cohort. Also, the rate of POI among women who did not have a bowel leak or abscess was 28.2%, similar to the overall cohort POI rate of 30.3%.

Whereas some risk factors for POI appear to be nonmodifiable, including sites and extent of carcinoma involvement at initial surgical exploration and preoperative platelet levels, this study has provided clues for factors that may be modifiable, including red blood cell transfusions. Not only was the percentage of patients receiving any red blood cell transfusion higher in those with POI, but also the proportion of patients with POI increased with increasing units of blood transfused. This suggests that judicious use of transfusions may favorably affect POI. Indeed, recent studies suggest blood transfusion is associated with adverse outcomes in various clinical and surgical contexts [34,35]. Additionally, although total postoperative intravenous narcotic doses were not different among those who did and did not have POI, the use of ibuprofen appeared to be associated with reduced risk of POI.

We may hypothesize that the use of oral ibuprofen was opioid-sparing and thus mitigated the negative GI effects of opioids [36]. However, we did not observe lower doses of intravenous narcotics in patients who received higher doses of ibuprofen. Additionally, given the potential adverse effect of nonsteroidal antiinflammatory drugs, the benefit-to-risk profile of ibuprofen requires consideration for each patient. Also, because of the tight range of daily narcotic dose when averaged over the hospital stay, differences in POI with regard

to the amount of intravenous narcotic use may have been difficult to detect. Detailed daily intravenous narcotic dosage during the first 72 h after surgery may have been more informative; daily quantification of opioid and ibuprofen use during the first 72 postoperative hours will be analyzed in a follow-up prospective study.

A limitation of this study was its retrospective nature and that we included only women undergoing primary cytoreduction. The rates of POI may be different among women who undergo interval cytoreduction after neoadjuvant chemotherapy or among women who undergo secondary cytoreduction. A strength of this study is that during the 6-year study period, practice patterns remained fairly constant among all gynecologic oncology surgeons, which limits the potential effect of practice evolution. Additionally, the characterization of the women who underwent more contemporary primary cytoreduction is comprehensive, allowing for identification of independent characteristics associated with POI. Also, during this time period, no interventions to enhance GI recovery were used and thus this study illustrates the natural history of GI recovery for this patient population.

Although straightforward modifiable risk factors were not identified on our analysis, attempts should be made to further decrease the risk of POI after EOC staging and debulking. Minimally invasive surgery is known to decrease surgical morbidity, including POI, which has been reported in the staging of ovarian borderline tumors and early-stage EOC [37,38]; the technique, however, has limitations in EOC and is not recommended for cytoreduction of advanced-stage disease [39,40]. Thorough assessment of peritoneal surfaces, as can only be assessed through visualization and palpation, is imperative in the surgical effort because residual disease decreases survival. Thus, laparotomy appears to be a mainstay of primary management of EOC, and alternative methods of decreasing postlaparotomy sequelae are required. In our study and in previous publications, POI has been associated with prolonged hospital LOS [21–23]. In addition, POI is associated with increased postoperative morbidity and higher hospital costs [21–23]. As such, it is possible that accelerating GI recovery may favorably affect overall surgical recovery and may decrease rates of other postoperative sequelae.

Acknowledgments

This was an investigator-initiated study supported in part by a grant from Adolor Corporation and GlaxoSmithKline. This work was also supported in part by the Office of Women's Health Research Building Interdisciplinary Careers in Women's Health (BIRCWH award K12 HD065987). The funding sources had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Amy Rachfal, PhD, Adolor Corporation, provided medical editorial assistance.

Abbreviations

BMI	body mass index
BR	bowel resection
EOC	epithelial ovarian cancer
FIGO	International Federation of Gynecology and Obstetrics
FTC	fallopian tube cancer
GI	gastrointestinal tract
IQR	interquartile range
LOS	length of stay

MSE	morphine sulfate equivalents
POI	postoperative ileus
PPC	primary peritoneal cancer

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin.* Sep-Oct;2010 60(5): 277–300. [Epub 2010 Jul 7]. Erratum in: *CA Cancer J Clin* Sep–Oct 2010;61(2):133–4. [PubMed: 20610543]
2. Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Relationship among surgical complexity, short-term morbidity, and overall survival in primary surgery for advanced ovarian cancer. *Am J Obstet Gynecol.* Dec; 2007 197(6):676, e1–7. [PubMed: 18060979]
3. Gillette-Cloven N, Burger RA, Monk BJ, McMeekin DS, Vasilev S, DiSaia PJ, et al. Bowel resection at the time of primary cytoreduction for epithelial ovarian cancer. *J Am Coll Surg.* Dec; 2001 193(6):626–32. [PubMed: 11768679]
4. Ozols RF, Bundy BN, Greer BE, Fowler JM, Clarke-Pearson D, Burger RA, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* Sep 1; 2003 21(17): 3194–200. [Epub 2003 Jul 14]. [PubMed: 12860964]
5. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med.* Jan 5; 2006 354(1):34–43. [PubMed: 16394300]
6. Eisenhauer EL, Abu-Rustum NR, Sonoda Y, Aghajanian C, Barakat RR, Chi DS. The effect of maximal surgical cytoreduction on sensitivity to platinum-taxane chemotherapy and subsequent survival in patients with advanced ovarian cancer. *Gynecol Oncol.* Feb; 2008 108(2):276–81. [Epub 2007 Dec 11]. [PubMed: 18063020]
7. Eisenhauer EL, Abu-Rustum NR, Sonoda Y, Levine DA, Poyner EA, Aghajanian C, et al. The addition of extensive upper abdominal surgery to achieve optimal cytoreduction improves survival in patients with stages IIIC–IV epithelial ovarian cancer. *Gynecol Oncol.* Dec; 2006 103(3):1083–90. [Epub 2006 Aug 4]. [PubMed: 16890277]
8. Chi DS, Eisenhauer EL, Zivanovic O, Sonoda Y, Abu-Rustum NR, Levine DA, et al. Improved progression-free and overall survival in advanced ovarian cancer as a result of a change in surgical paradigm. *Gynecol Oncol.* Jul; 2009 114(1):26–31. [Epub 2009 Apr 23]. [PubMed: 19395008]
9. Mourtun SM, Temple LK, Abu-Rustum NR, Gemignani ML, Sonoda Y, Bochner BH, et al. Morbidity of rectosigmoid resection and primary anastomosis in patients undergoing primary cytoreductive surgery for advanced epithelial ovarian cancer. *Gynecol Oncol.* Dec; 2005 99(3):608–14. [Epub 2005 Sep 8]. [PubMed: 16153697]
10. Peiretti M, Zanagnolo V, Aletti GD, Bocciolone L, Colombo N, Landoni F, et al. Role of maximal primary cytoreductive surgery in patients with advanced epithelial ovarian and tubal cancer: surgical and oncological outcomes. Single institution experience. *Gynecol Oncol.* Nov; 2010 119(2):259–64. [Epub 2010 Aug 25]. [PubMed: 20800269]
11. Shih KK, Chi DS, Barakat RR, Leitao MM Jr. Tertiary cytoreduction in patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer: an updated series. *Gynecol Oncol.* May; 2010 117(2):330–5. [Epub 2010 Feb 26]. [PubMed: 20189234]
12. Katsumata N, Yasuda M, Takahashi F, Isonishi S, Jobo T, Aoki D, et al. Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer: a phase 3, open-label, randomised controlled trial. *Lancet.* Oct 17; 2009 374(9698):1331–8. [Epub 2009 Sep 18]. [PubMed: 19767092]
13. Richardson DL, Mariani A, Cliby WA. Risk factors for anastomotic leak after rectosigmoid resection for ovarian cancer. *Gynecol Oncol.* Nov; 2006 103(2):667–72. [Epub 2006 Jun 23]. [PubMed: 16797684]

14. Tebes SJ, Cardosi R, Hoffman MS. Colorectal resection in patients with ovarian and primary peritoneal carcinoma. *Am J Obstet Gynecol.* Aug; 2006 195(2):585–9. [Epub 2006 May 30]. [PubMed: 16730631]
15. Webb MJ, Weaver EW. Intestinal surgery in gynaecological oncology. *Aust N Z J Obstet Gynaecol.* Nov; 1987 27(4):299–303. [PubMed: 3453666]
16. Elattar A, Bryant A, Winter-Roach BA, Hatem M, Naik R. Optimal primary surgical treatment for advanced epithelial ovarian cancer. *Cochrane Database Syst Rev.* Aug 10.2011 (8):CD007565. [PubMed: 21833960]
17. Shih KK, Chi DS. Maximal cytoreductive effort in epithelial ovarian cancer surgery. *J Gynecol Oncol.* Jun; 2010 21(2):75–80. [Epub 2010 Jun 30]. [PubMed: 20613895]
18. Woods JH, Erickson LW, Condon RE, Schulte WJ, Sillin LF. Postoperative ileus: a colonic problem? *Surgery.* Oct; 1978 84(4):527–33. [PubMed: 99829]
19. Wilson JP. Postoperative motility of the large intestine in man. *Gut.* Sep; 1975 16(9):689–92. [PubMed: 1193424]
20. Fagotti A, Fanfani F, Ercoli A, Giordano MA, Sallustio G, Scambia G. Postoperative ileus after para-aortic lymphadenectomy: a prospective study. *Gynecol Oncol.* Jan; 2007 104(1):46–51. [Epub 2006 Aug 21]. [PubMed: 16919717]
21. Iyer S, Saunders WB, Stemkowski S. Economic burden of postoperative ileus associated with colectomy in the United States. *J Manag Care Pharm.* Jul-Aug;2009 15(6):485–94. [PubMed: 19610681]
22. Chang SS, Baumgartner RG, Wells N, Cookson MS, Smith JA Jr. Causes of increased hospital stay after radical cystectomy in a clinical pathway setting. *J Urol.* Jan; 2002 167(1):208–11. [PubMed: 11743307]
23. Schuster TG, Montie JE. Postoperative ileus after abdominal surgery. *Urology.* Apr; 2002 59(4):465–71. [PubMed: 11927292]
24. Salvador CG, Sikrica M, Evans A, Pizzi L, Goldfarb N. Clinical and economic outcomes of prolonged postoperative ileus in patients undergoing hysterectomy and hemicolectomy. *P & T.* Oct; 2005 30(10):590–5.
25. Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery.* Jun; 2011 149(6):830–40. [Epub 2011 Jan 14]. [PubMed: 21236454]
26. Kariv Y, Delaney CP, Senagore AJ, Manilich EA, Hammel JP, Church JM, et al. Clinical outcomes and cost analysis of a “fast track” postoperative care pathway for ileal pouch-anal anastomosis: a case control study. *Dis Colon Rectum.* Feb; 2007 50(2):137–46. [PubMed: 17186427]
27. Tsikitis VL, Holubar SD, Dozois EJ, Cima RR, Pemberton JH, Larson DW. Advantages of fast-track recovery after laparoscopic right hemicolectomy for colon cancer. *Surg Endosc.* Aug; 2010 24(8):1911–6. [Epub 2010 Jan 28]. [PubMed: 20108142]
28. Andersen HK, Lewis SJ, Thomas S. Early enteral nutrition within 24h of colorectal surgery versus later commencement of feeding for postoperative complications. *Cochrane Database Syst Rev.* Oct 18.2006 (4):CD004080. [PubMed: 17054196]
29. Marx C, Rasmussen T, Jakobsen DH, Ottosen C, Lundvall L, Ottesen B, et al. The effect of accelerated rehabilitation on recovery after surgery for ovarian malignancy. *Acta Obstet Gynecol Scand.* 2006; 85(4):488–92. [PubMed: 16612713]
30. Jakobsen DH, Hogdall C, Kehlet H. Perioperative care of patients with stage IIIC ovarian cancer. *Ugeskr Laeger.* Sep 27; 2010 172(39):2688–91. [Danish]. [PubMed: 20920397]
31. Hall BL, Hamilton BH, Richards K, Bilimoria KY, Cohen ME, Ko CY. Does surgical quality improve in the American College of Surgeons National Surgical Quality Improvement Program: an evaluation of all participating hospitals. *Ann Surg.* Sep; 2009 250(3):363–76. [PubMed: 19644350]
32. Khuri SF, Daley J, Henderson WG. The comparative assessment and improvement of quality of surgical care in the Department of Veterans Affairs. *Arch Surg.* Jan; 2002 137(1):20–7. [PubMed: 11772210]

33. American Pain Society. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain. 6th ed.. American Pain Society; Glenview (IL): 2008.
34. Bhaskar B, Bidstrup BP, Fung YL, Fraser JF. To transfuse, or not to transfuse: that is the question. *Crit Care Resusc.* Mar; 2009 11(1):71–7. [PubMed: 19281448]
35. Carless PA, Henry DA, Carson JL, Hebert PP, McClelland B, Ker K. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. *Cochrane Database Syst Rev.* Oct 6, 2010 (10):CD002042. [PubMed: 20927728]
36. Beard TL, Leslie JB, Nemeth J. The opioid component of delayed gastrointestinal recovery after bowel resection. *J Gastrointest Surg.* Jul; 2011 15(7):1259–68. [Epub 2011 Apr 15]. [PubMed: 21494914]
37. Chi DS, Abu-Rustum NR, Sonoda Y, Ivy J, Rhee E, Moore K, et al. The safety and efficacy of laparoscopic surgical staging of apparent stage I ovarian and fallopian tube cancers. *Am J Obstet Gynecol.* May; 2005 192(5):1614–9. [PubMed: 15902166]
38. Nezhat FR, Ezzati M, Chuang L, Shamshirsaz AA, Rahaman J, Gretz H. Laparoscopic management of early ovarian and fallopian tube cancers: surgical and survival outcome. *Am J Obstet Gynecol.* Jan; 2009 200(1):83, e1–6. Epub 2008 Nov 18. [PubMed: 19019337]
39. Iglesias DA, Ramirez PT. Role of minimally invasive surgery in staging of ovarian cancer. *Curr Treat Options Oncol.* Sep; 2011 12(3):217–29. [PubMed: 21503633]
40. Spirtos NM, Eisekop SM, Boike G, Schlaerth JB, Cappellari JO. Laparoscopic staging in patients with incompletely staged cancers of the uterus, ovary, fallopian tube, and primary peritoneum: a Gynecologic Oncology Group (GOG) study. *Am J Obstet Gynecol.* Nov; 2005 193(5):1645–9. [PubMed: 16260204]

Box 1**Surgical complexity scoring.**

Procedure	Points
Total hysterectomy + bilateral salpingo-oophorectomy	1
Omentectomy	1
Pelvic lymphadenectomy	1
Para-aortic lymphadenectomy	1
Pelvic peritoneum stripping	1
Abdominal peritoneum stripping	1
Rectosigmoidectomy, T-T anastomosis	3
Large bowel resection	2
Diaphragm stripping and resection	2
Splenectomy	2
Liver resection	2
Small bowel resection	1

Complexity score groups	Points
1 – Low	3
2 – Intermediate	4–7
3 – High	8

Adapted from Aletti et al. [2]. Used with permission.

Fig. 1. Incidence of POI by number of perioperative red blood cell transfusions. All P values by Cochran-Armitage trend test. Intraop indicates intraoperative; Postop, postoperative.

Table 1

Patient demographics and baseline characteristics (N = 587).

Characteristic	Value ^a
Age at surgery, y	63.8 (11.7) [33.3–90.7]
BMI, kg/m ² (n = 585)	28.1 (6.4) [16.5–56.0]
BMI category (n = 585)	
Underweight/normal (< 24.9)	213 (36.4)
Overweight (25.0–29.9)	181 (30.9)
WHO class I (30.0–34.9)	106 (18.1)
WHO class II (35.0–39.9)	48 (8.2)
WHO class III/super (> 40.0)	37 (6.3)
ECOG performance status	
0/1	535 (91.1)
2/3	49 (8.4)
4	2 (0.3)
Unknown	1 (0.2)
ASA score	
1/2	312 (53.2)
3/4	275 (46.8)
Platelets, ×10 ⁹ /L (n = 578)	376.9 (146.3) [115.0–1392.0]
Platelets >400 × 10 ⁹ /L (n = 578)	192 (33.2)
CA-125, U/mL (n = 560)	1847.4 (4105.0) [3.5–45,400]
Albumin, g/dL	3.9 (0.6) [1.9–5.0]
Comorbid conditions	
Hypertension	270 (46.0)
Current/past smoker	226 (38.5)
Hyperlipidemia	223 (38.0)
GERD	159 (27.1)
Preoperative anemia (hemoglobin <12 g/dL)	184 (31.3)
Hypothyroidism	106 (18.1)
Type II diabetes mellitus	58 (9.9)
Coronary artery disease	46 (7.8)
Prior DVT/PE	45 (7.7)
Asthma	41 (7.0)
History of stroke/TIA	30 (5.1)
COPD/emphysema	26 (4.4)
Prior hysterectomy	138 (23.5)

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; GERD, gastroesophageal reflux disease; PE, pulmonary embolism; TIA, transient ischemic attack; WHO, World Health Organization.

^aValues are mean (SD) [range] or No. of patients (%).

Table 2

Operative findings, intraoperative process-of-care variables, and postoperative pain management (N = 587).

Variable	Value ^a
Primary carcinoma diagnosis	
Epithelial ovarian	434 (73.9)
Primary peritoneal	118 (20.1)
Fallopian tube	35 (6.0)
Extent of carcinoma involvement at initial exploration	
Omentum	365 (62.2)
Bowel serosa	356 (60.6)
Cul-de-sac	293 (49.9)
Diaphragm	286 (48.7)
Bowel mesentery	271 (46.2)
Bladder peritoneum	176 (30.0)
Liver parenchyma	34 (5.8)
Ascites	336 (57.2)
FIGO stage	
Early (stage I/II)	129 (22.0)
Advanced (stage IIIA)	458 (78.0)
FIGO grade	
1/2	65 (11.1)
3	522 (88.9)
Histology	
Serous	391 (66.6)
Endometrioid	59 (10.1)
Mixed	42 (7.2)
Clear cell	30 (5.1)
Mucinous	23 (3.9)
Other adenocarcinoma, NOS	20 (3.4)
Carcinosarcoma	19 (3.2)
Undifferentiated	2 (0.3)
Squamous	1 (0.2)
Positive lymph nodes	
Pelvic ^b	201 (43.3)
Para-aortic ^c	186 (41.5)
Residual disease	
Microscopic	316 (53.8)
Cytoreduction <1 cm measurable residual	184 (31.4)
Cytoreduction 1 cm residual	87 (14.8)
Surgical procedures performed	
Hysterectomy	439 (74.8)

Variable	Value ^a
Unilateral or bilateral salpingo-oophorectomy	568 (96.8)
Pelvic lymphadenectomy	464 (79.0)
Para-aortic lymphadenectomy	448 (76.3)
Omentectomy	569 (96.9)
Pelvic peritoneal stripping	246 (41.9)
Any bowel resection	205 (34.9)
Low anterior resection/reanastomosis	160 (27.3)
Other large bowel resection	63 (10.7)
Small bowel resection	50 (8.5)
Diaphragm stripping/resection	157 (26.7)
Appendectomy	212 (36.1)
Splenectomy	76 (12.9)
Liver resection	17 (2.9)
Surgical complexity	
Low	104 (17.7)
Intermediate	347 (59.1)
High	136 (23.2)
Estimated blood loss, mL	979.9 (800.6) [30–6500]
Red blood cell transfusion	452 (77.0)
Intraoperative only	146 (24.9)
Postoperative only	99 (16.9)
Intraoperative and postoperative	207 (35.3)
Daily postoperative IV narcotics, MSE mg ^d	19.8 (25.7) [0–314.3]
Any postoperative ibuprofen	348 (59.3)

Abbreviations: FIGO, Federation of Gynecology and Obstetrics; IV, intravenous; MSE, morphine sulfate equivalents; NOS, not otherwise specified.

^aValues are mean (SD) [range] or No. of patients (%).

^bBased on 464 patients undergoing pelvic lymphadenectomy.

^cBased on 448 patients undergoing para-aortic lymphadenectomy.

^dFive patients did not use any IV narcotics.

Table 3

Univariate analysis for variables associated with POI after primary cytoreduction for epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer.

Variable	Patient group ^a		P Value ^b
	Without POI ^c (n = 409)	With POI ^c (n = 178)	
Mean (SD) age, y	63.1 (11.5)	65.3 (12.0)	.04
Median (IQR) CA-125, U/mL	471 (133–1308)	733 (200–2265)	.004
Preoperative thrombocytosis (platelet count >400 × 10 ⁹ /L)	116 (28.4)	76 (42.7)	.001
Extent of carcinoma involvement at initial exploration			
Omentum	242 (59.2)	123 (69.1)	.02
Bowel serosa	235 (57.5)	121 (68.0)	.02
Cul-de-sac	189 (46.2)	104 (58.4)	.007
Diaphragm	181 (44.3)	105 (59.0)	.001
Bowel mesentery	166 (40.6)	105 (59.0)	<.001
Bladder peritoneum	109 (26.7)	67 (37.6)	.008
Liver parenchyma	18 (4.4)	16 (9.0)	.03
Ascites	215 (52.6)	121 (68.0)	<.001
FIGO stage			.001
Early (stage I/II)	105 (25.7)	24 (13.5)	
Advanced (stage IIIA)	304 (74.3)	154 (86.5)	
Positive lymph nodes			
Pelvic ^d	129/326 (39.6)	72/138 (52.2)	.01
Para-aortic ^e	118/316 (37.3)	68/132 (51.5)	.006
Residual disease grouping			.001
Microscopic	239 (58.4)	77 (43.3)	
Cytoreduction <1 cm measurable residual	120 (29.3)	64 (36.0)	
Cytoreduction ≥1 cm residual	50 (12.2)	37 (20.8)	
Concomitant surgical procedure			
Hysterectomy	316 (77.3)	123 (69.1)	.04
Any bowel resection	126 (30.8)	79 (44.4)	.002
Low anterior resection/reanastomosis	94 (23.0)	66 (37.1)	<.001
Other large bowel resection	35 (8.6)	28 (15.7)	.01
Small bowel resection	28 (6.8)	22 (12.4)	.03
Surgical complexity			.01
Low	74 (18.1)	30 (16.9)	
Intermediate	254 (62.1)	93 (52.2)	
High	81 (19.8)	55 (30.9)	
Any red blood cell transfusion	297 (72.6)	155 (87.1)	<.001
Any postoperative ibuprofen	271 (66.3)	77 (43.3)	<.001

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; IQR, interquartile range; POI, postoperative ileus.

^aValues are no. of patients (%) unless otherwise stated.

^b P values based on the 2-sample t test for age, Wilcoxon rank sum test for CA-125, and the χ^2 test for all other variables.

^c POI was defined as surgeon diagnosis of POI, return to nothing-by-mouth status, or reinsertion of a nasogastric tube.

^d Based on 464 total patients undergoing pelvic lymphadenectomy.

^e Based on 448 total patients undergoing para-aortic lymphadenectomy.

Table 4

Multivariate analysis of independent risk factors for POI after primary cytoreduction for epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer.^a

Variable	Odds ratio (95% CI)	P value
Preoperative thrombocytosis (platelet count $>400 \times 10^9/L$)	1.49 (1.01–2.19)	.045
Carcinoma involvement of bowel mesentery at initial exploration	1.68 (1.15–2.45)	.007
Any red blood cell transfusion	1.96 (1.17–3.28)	.01
Any postoperative ibuprofen	0.43 (0.30–0.62)	<.001

Abbreviation: POI, postoperative ileus.

^a All variables listed in Table 3 were included in the multivariate analysis. Additional variables with .05 $P < .20$ not listed in Table 3 but included in the multivariate analysis were body mass index class; hypertension; current or past smoking status; coronary artery disease; chronic obstructive pulmonary disease or emphysema; history of hysterectomy; concomitant surgical procedures of omentectomy, pelvic peritoneal stripping, and diaphragm stripping or resection; and mean estimated blood loss.