

Predictors and Clinical Consequences of Postoperative Morbidity Following Cytoreductive Surgery for Advanced-Stage Epithelial Ovarian Cancer

Pooja Singh¹, Navin Kumar²

¹Assistant Professor, Department of Gynaecology Oncology, Patna medical college and Hospital, Patna, Bihar, India

²Assistant Professor, Department of Surgical Oncology, Patna medical college and Hospital, Patna, Bihar, India

Received: 05-03-2026 / Revised: 20-04-2026 / Accepted: 30-05-2026

Corresponding Author: Dr. Navin Kumar

Conflict of interest: Nil

Abstract:

Background: Cytoreductive surgery is a cornerstone of treatment for advanced-stage epithelial ovarian cancer, but extensive surgical procedures may result in substantial postoperative morbidity and can delay subsequent systemic therapy. Identifying predictors of postoperative complications is therefore important for perioperative risk stratification and treatment planning.

Aim: To identify predictors of postoperative morbidity following cytoreductive surgery for advanced-stage epithelial ovarian cancer and evaluate its clinical consequences, particularly delayed initiation of adjuvant chemotherapy.

Methodology: This retrospective observational study included 60 women with FIGO stage III–IV epithelial ovarian cancer who underwent cytoreductive surgery at Patna Medical College and Hospital, Bihar, India. Demographic, clinical, laboratory, and perioperative variables were extracted from medical records. Postoperative complications occurring during hospitalization or within 30 days were assessed using the Clavien–Dindo classification. Univariable and multivariable logistic regression analyses were performed to identify predictors of postoperative morbidity. Chemotherapy initiation beyond 42 days was considered delayed.

Result: Postoperative complications occurred in 10 patients. Older age, longer operative duration, lower albumin, higher ASA status, bowel surgery, perioperative and postoperative blood transfusion, and anterior peritonectomy were associated with morbidity on initial analysis. Perioperative blood transfusion was the only independent predictor (OR 3.86, 95% CI 1.06–14.72; $p=0.041$). Major complications included intra-abdominal abscess, bleeding, anastomotic leak, intestinal perforation, thromboembolism, acute kidney injury, severe wound infection, and mortality. Delayed chemotherapy was associated with postoperative complications, longer hospitalization, longer surgery, lower albumin, higher Aletti score, and more frequent bowel surgery.

Conclusion: Postoperative morbidity is clinically important following extensive cytoreductive surgery and may delay chemotherapy. Preoperative optimization, careful surgical planning, blood-conservation strategies, and close postoperative monitoring may improve recovery and facilitate timely systemic treatment.

Keywords: Epithelial Ovarian Cancer; Cytoreductive Surgery; Postoperative Morbidity; Surgical Complications; Perioperative Transfusion; Chemotherapy Delay; Clavien–Dindo Classification; Ovarian Cancer.

DOI: 10.25258/ijpqa.17.5.75

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Ovarian cancer is one of the most aggressive gynecological cancers and a great challenge in women's health due to its aggressive biological behavior, unspecific initial symptoms and advanced stage at diagnosis. Cancer statistics released in 2022 show that over 324,000 new cases of ovarian cancer were reported globally and over 206,000 people lost their lives due to ovarian cancer in a span of just one year. Often the presentation is nonspecific with symptoms of fatigue, abdominal distension, bowel or urinary changes, and abdominal or pelvic discomfort [1]. These signs and symptoms could be mistaken for

those of a "harmless" disorder of the gastrointestinal, urinary or gynecological tract, so the diagnosis is often delayed until the tumour has grown out of the pelvis. Thus, a significant number of patients are diagnosed with International Federation of Obstetrics and Gynecology (FIGO) Stage III or IV disease with widespread peritoneal, abdominal or distant dissemination [2]. Advanced stage presentation is still an important factor for poor prognosis and is a significant factor in the low long-term survival for epithelial ovarian cancer.

Most ovarian cancers are of epithelial origin and the best treatment for advanced disease is a multimodal approach, which usually involves surgery and systemic chemotherapy. Cytoreductive surgery is a key part of treatment, and the main goal of surgery is complete macroscopic resection of all visible tumor deposits [3]. Residual disease post-surgery has a strong correlation to oncologic outcomes and complete cytoreduction has always been identified as a significant predictor of survival rates. In the more advanced disease, however, the procedures to obtain complete cytoreduction are often long and technically challenging, and may involve surgery of the bowel, diaphragm, spleen, liver, or urinary tract. The heightened risks of increased aggressiveness and complexity of the surgery may thus present significant perioperative risk, especially when complicated by a large burden of disease, poor nutritional status, advanced age, comorbid illness, and poor functional reserve.

Primary debulking surgery (PDS) followed by systemic chemotherapy is recommended in patients with advanced-stage epithelial ovarian cancer (FIGO stage III–IV) who are surgical candidates and in whom optimal cytoreduction is thought to be attainable, per the National Comprehensive Cancer Network (NCCN) guidelines. In contrast, neoadjuvant chemotherapy (NACT) and interval debulking surgery (IDS) should be used for patients who are not candidates to undergo extensive primary surgery and/or those with a poor chance of achieving optimal cytoreduction at initial laparotomy. Primary debulking surgery might be used in the early stages to achieve complete tumor clearance, but complete cytoreduction may need to involve aggressive surgery with potential high postoperative morbidity [4]. In patients who have complete cytoreduction at PDS, better survival is reported [5]. IDS after NACT on the other hand is more "economical" and less complex, as chemotherapy might downsize a tumor making the surgery easier. There is currently a great deal of debate on whether PDS or IDS results in a greater relative survival advantage, but a number of studies have demonstrated similar outcomes in carefully selected patients. These findings highlight the need for tailoring the choice of treatment to the patient, the extent of disease, the complexity of surgery, and the chances of acceptable cytoreduction.

Postoperative morbidity is an important clinical consequence of cytoreductive surgery and can significantly affect the treatment path. Postoperative infection, wound complications, bleeding, thromboembolic complications, gastrointestinal complications, anastomotic leakage, urinary complications, respiratory morbidity, and prolonged ileus can lead to prolonged hospital stays, higher rates of health care utilization, slower recovery, and decrease in functional status. Of note, postoperative complications can also impact the ability to initiate systemic anticancer

treatment in a timely fashion [6]. This is especially true in patients with advanced ovarian cancer, where surgery is only part of the treatment and the benefit of cytoreduction relies on the following administration of the appropriate chemotherapy. Multiple studies have shown that a delay in beginning adjuvant chemotherapy treatment can have a negative impact on prognosis [7]. The time between the surgical procedure and the start of chemotherapy remains controversial; however, starting chemotherapy within about 6 weeks after surgery, to make treatment easier and possibly more effective in terms of oncological outcomes, is recommended [8].

Various factors interact affecting the development of postoperative morbidity. Pre-operative factors like age, nutritional status, anemia, comorbidities, performance status, stage of disease, disease burden, ascites, and prior treatments can impact a patient's ability to tolerate large amounts of surgery. Operative factors such as length of surgery, blood loss, amount of peritoneal disease, number of organs respected, type of organs respected, bowel surgery, and complete cytoreduction may also play a role in postoperative complications. These factors are more significant when a patient has high stage epithelial ovarian cancer, and the surgical goal is complete removal of the tumor which may involve surgery beyond that of the gynecologist [9]. Thus, the preoperative identification of patients at high risk for postoperative morbidity may allow clinicians to optimize modifiable risk factors, facilitate perioperative planning, select appropriate surgical patients, advise patients on expected outcomes, and choose alternative treatments, when indicated.

Postoperative morbidity has clinical importance beyond the immediate postoperative period. These complications can increase the length of hospital stay and recovery, delay the start of additional chemotherapy, and make it difficult to continue multimodal treatment of cancer. In a resource-limited environment like Bihar, India, where patients can come in with advanced disease and the availability of health care resources is quite variable, identifying patients at high risk for postoperative complications is very important. Closer appreciation of the factors that predict morbidity may help to optimize the patient preoperatively, multidisciplinary decision-making, efficient use of peri-operative resources, and the closer monitoring of the patient post-operatively. Additionally, an analysis of the incidence of postoperative complications and their relation to the time chemotherapy was started could give clinically relevant data about how surgical morbidity might influence the postoperative oncologic management.

However, despite the improvement of surgical technique, peri-operative care and systemic treatment, postoperative morbidity is still an important determinant of recovery following cytoreductive surgery for advanced ovarian cancer. Hence, the need to

identify easily measurable, pre- and peri-operative parameters which are associated with higher morbidity rates and understand the impact of these complications on the subsequent delivery of treatment. Therefore, the current retrospective study was conducted to assess the pre- and post-operative morbidity factors of the cytoreductive surgery for advanced stage EOC in Bihar, India. Specific objectives of the study were to determine patient- and disease-specific factors related to postoperative complications, the relationship between postoperative morbidity and time to initiation of adjuvant chemotherapy and the potential clinical implications of delayed postoperative chemotherapy. This study aims to improve the perioperative risk assessment, plan treatment accordingly, start systemic treatment in time, and manage women undergoing cytoreductive surgery for advanced stage epithelial ovarian cancer better by identifying patient groups at high risk and clinically relevant predictors of morbidity.

Methodology

Study Design: This study was designed as a retrospective observational study to evaluate predictors and clinical consequences of postoperative morbidity following cytoreductive surgery for advanced-stage epithelial ovarian cancer.

Study Setting: The study was conducted in the Department of Gynaecology Oncology, Patna Medical College and Hospital, Patna, Bihar, India.

Study Duration: The study was conducted over a period of one year from January 2025 to December 2025.

Study Population: The study population consisted of adult women diagnosed with advanced-stage epithelial ovarian cancer who underwent cytoreductive surgery during the study period. Advanced disease was defined as FIGO stage III or IV epithelial ovarian cancer according to the applicable FIGO staging system.

Sample Size: A total of 60 patients were included in the study. Based on the occurrence of postoperative morbidity, patients were divided into two groups: 50 patients without postoperative complications and 10 patients with postoperative complications.

Inclusion Criteria

Patients were included if they fulfilled all of the following criteria:

- Women aged 18 years or older.
- Histopathologically confirmed epithelial ovarian cancer.
- FIGO stage III or IV disease.
- Underwent cytoreductive surgery at Patna Medical College and Hospital during the study period.

- Availability of adequate demographic, clinical, operative, and postoperative information in the medical records.

Exclusion Criteria

Patients were excluded if they had:

- A previous history of another malignancy.
- Incomplete or inadequate medical records.
- Missing essential preoperative or postoperative information.
- Inability to determine the occurrence or severity of postoperative complications.
- A diagnosis other than epithelial ovarian carcinoma.
- Any other condition that prevented reliable assessment of the predefined study outcomes.

Data Collection and Study Variables: Relevant information was extracted from hospital medical records using a structured data collection proforma. The collected variables included demographic characteristics, clinical presentation, comorbidities, preoperative performance status, disease stage, histopathological characteristics, and preoperative laboratory parameters. Laboratory investigations performed within seven days before surgery were considered for evaluating the patients' preoperative clinical and nutritional status.

Surgical variables included the type of cytoreductive surgery, primary debulking surgery or interval debulking surgery following neoadjuvant chemotherapy, duration of surgery, estimated intraoperative blood loss, need for blood transfusion, extent of surgical procedures, residual disease after cytoreduction, and degree of surgical complexity. The Aletti surgical complexity score was used, where documentation permitted, to classify surgical procedures into low complexity (score ≤ 3), intermediate complexity (score 4–7), and high complexity (score ≥ 8).

Postoperative variables included the occurrence and type of complications, severity of complications, duration of hospital stay, requirement for intensive care, need for reoperation or additional interventions, and the time taken to initiate postoperative chemotherapy. These variables were assessed to determine the factors associated with postoperative morbidity and its clinical consequences.

Assessment of Postoperative Complications: The primary outcome was the occurrence of postoperative complications following cytoreductive surgery. Complications documented during the postoperative hospital stay and within 30 days after surgery were considered for outcome assessment, wherever follow-up information was available. The Clavien–Dindo classification system was used to grade the severity of postoperative complications according to

the treatment or intervention required for their management.

Complications were classified as minor or major according to their severity. Clavien–Dindo grades I and II represented complications managed with conservative treatment or pharmacological interventions, whereas grades III and IV represented complications requiring surgical, endoscopic, radiological, or intensive care interventions. Grade V represented death. Severe postoperative morbidity was defined as a Clavien–Dindo grade III or higher complication. The types of complications assessed included postoperative infection, wound-related complications, hemorrhage, thromboembolic events, gastrointestinal complications, urinary tract complications, and other documented medical or surgical adverse events.

Patients were classified into the no-complication group ($n = 50$) and the complication group ($n = 10$) according to the presence or absence of documented postoperative morbidity. The relationship between preoperative patient characteristics, disease-related factors, surgical complexity, and postoperative complications was subsequently evaluated.

Assessment of Clinical Consequences

The secondary outcomes included the clinical consequences of postoperative complications, particularly prolonged hospitalization, intensive care unit admission, reoperation, requirement for additional interventions, and delay in the initiation of adjuvant chemotherapy. The duration of hospital stay was calculated from the date of surgery to the date of discharge.

Delayed initiation of adjuvant chemotherapy was defined as commencement of chemotherapy more than 42 days after surgery. This six-week threshold was used to evaluate the potential effect of postoperative morbidity on the timely continuation of oncological treatment. Information regarding the date of chemotherapy initiation was obtained from postoperative treatment records, wherever available. Other clinical consequences were assessed based on documented postoperative events and follow-up records.

Statistical Analysis: Data were entered into a structured database and analyzed using appropriate statistical software. Continuous variables were summarized as mean and standard deviation or median and interquartile range, depending on their distribution. Normality was assessed using graphical methods and the Shapiro–Wilk test. Categorical variables were expressed as frequencies and percentages.

Comparisons between patients with and without postoperative complications were performed using the independent-samples Student's *t*-test for normally distributed continuous variables or the Mann–Whitney *U* test for non-normally distributed

variables. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate, particularly when expected cell frequencies were small.

Univariable logistic regression analysis was used to evaluate associations between relevant demographic, clinical, laboratory, disease-related, and surgical factors and the occurrence of postoperative complications. Where the number of outcome events permitted, clinically relevant variables were considered for multivariable logistic regression to identify independent predictors of postoperative morbidity. Associations were expressed as odds ratios with corresponding 95% confidence intervals. Given the relatively small number of patients experiencing complications, multivariable analyses were interpreted cautiously to minimize the risk of model overfitting.

A two-sided *p*-value of less than 0.05 was considered statistically significant. The findings were interpreted in the context of the retrospective study design, the available medical record documentation, and the limited sample size.

Result

Table 1 compares baseline and perioperative characteristics between patients without postoperative complications ($n=50$) and those with complications ($n=10$). Patients who developed complications were significantly older than those without complications, with median ages of 65.50 [59.00–71.00] and 58.00 [51.00–65.00] years, respectively ($p=0.041$). The median operation time was also significantly longer among patients with complications (300 [250–360] vs 235 [190–290] minutes, $p=0.018$), while median albumin was significantly lower (37.50 [34.00–42.00] vs 42.00 [39.00–45.00] g/L, $p=0.029$). Regarding ASA classification, ASA 3–4 was more frequent among patients with complications (70.0% vs 40.0%, $p=0.047$). Bowel surgery was significantly more common in the complication group (50.0% vs 18.0%, $p=0.006$), as were perioperative blood transfusion (70.0% vs 36.0%, $p=0.004$) and postoperative blood transfusion (70.0% vs 38.0%, $p=0.018$). Anterior peritonectomy was also significantly more frequent among patients with complications (40.0% vs 14.0%, $p=0.041$). The distribution of Aletti scores differed significantly between groups ($p=0.021$), with a higher proportion of score 3 among patients with complications (40.0% vs 14.0%). In contrast, BMI, hemoglobin, white blood cell count, platelet count, lymphocyte and neutrophil counts, CA125, tumor size, menopause, parity, diabetes mellitus, hypertension, previous abdominal surgery, surgery type, HIPEC, ascites, suboptimal cytoreduction, pleural effusion, omental cake, peritoneal carcinomatosis, pelvic peritonectomy, diaphragmatic peritonectomy, and FIGO stage did not differ significantly between the groups ($p>0.05$). Overall, postoperative complications were associated with older

age, longer operative duration, lower albumin, higher ASA category, bowel surgery, blood

transfusion, anterior peritonectomy, and higher Aletti score.

Table 1: Baseline and perioperative characteristics

Table 1: Baseline and perioperative characteristics			
Variable	No complication (n=50)	With complication (n=10)	p-value
Age (years)	58.00 [51.00, 65.00]	65.50 [59.00, 71.00]	0.041
BMI (kg/m²)	27.20 [24.30, 30.60]	25.10 [22.90, 28.40]	0.087
Operation time (min)	235.00 [190.00, 290.00]	300.00 [250.00, 360.00]	0.018
Hemoglobin (g/dL)	11.30 [10.20, 12.20]	10.80 [9.80, 11.60]	0.184
White blood cell count (×10 ⁹ /L)	6.40 [5.10, 8.00]	7.10 [5.80, 9.20]	0.238
Platelet count (×10 ⁹ /L)	265.00 [215.00, 325.00]	220.00 [180.00, 290.00]	0.112
Lymphocyte count (×10 ⁹ /L)	1.80 [1.30, 2.30]	1.60 [1.20, 2.10]	0.376
Neutrophil count (×10 ⁹ /L)	3.60 [2.70, 5.10]	4.60 [3.50, 5.80]	0.091
Albumin (g/L)	42.00 [39.00, 45.00]	37.50 [34.00, 42.00]	0.029
CA125 (U/ml)	68.50 [25.00, 245.00]	145.00 [48.00, 620.00]	0.072
Tumor size (cm)	5.00 [3.00, 9.00]	6.50 [4.00, 11.00]	0.148
Menopause			
No	10 (20.0)	1 (10.0)	0.213
Yes	40 (80.0)	9 (90.0)	
Parity			
No	4 (8.0)	0 (0.0)	0.612
Yes	46 (92.0)	10 (100.0)	
Diabetes mellitus			
No	39 (78.0)	7 (70.0)	0.681
Yes	11 (22.0)	3 (30.0)	
Hypertension			
No	33 (66.0)	5 (50.0)	0.421
Yes	17 (34.0)	5 (50.0)	
Previous abdominal surgery			
None	37 (74.0)	7 (70.0)	0.735
Pfannenstiel	10 (20.0)	2 (20.0)	
Midline laparotomy	3 (6.0)	1 (10.0)	
Surgery type			
PDS	18 (36.0)	4 (40.0)	0.724
IDS	32 (64.0)	6 (60.0)	
ASA score			
ASA 1–2	30 (60.0)	3 (30.0)	0.047
ASA 3–4	20 (40.0)	7 (70.0)	
HIPEC			
No	46 (92.0)	9 (90.0)	0.619
Yes	4 (8.0)	1 (10.0)	
Ascites			
No	40 (80.0)	6 (60.0)	0.157
Yes	10 (20.0)	4 (40.0)	
Bowel surgery			
No	41 (82.0)	5 (50.0)	0.006
Yes	9 (18.0)	5 (50.0)	
Suboptimal cytoreduction			
No	47 (94.0)	8 (80.0)	0.118
Yes	3 (6.0)	2 (20.0)	
Perioperative blood transfusion			
No	32 (64.0)	3 (30.0)	0.004
Yes	18 (36.0)	7 (70.0)	
Postoperative blood transfusion			
No	31 (62.0)	3 (30.0)	0.018
Yes	19 (38.0)	7 (70.0)	
Pleural effusion			

No	41 (82.0)	7 (70.0)	0.213
Yes	9 (18.0)	3 (30.0)	
Omental cake			
No	20 (40.0)	3 (30.0)	0.291
Yes	30 (60.0)	7 (70.0)	
Peritoneal carcinomatosis			
No	18 (36.0)	3 (30.0)	0.455
Yes	32 (64.0)	7 (70.0)	
Anterior peritonectomy			
No	43 (86.0)	6 (60.0)	0.041
Yes	7 (14.0)	4 (40.0)	
Pelvic peritonectomy			
No	40 (80.0)	6 (60.0)	0.074
Yes	10 (20.0)	4 (40.0)	
Diaphragmatic peritonectomy			
No	40 (80.0)	6 (60.0)	0.183
Yes	10 (20.0)	4 (40.0)	
Aletti score			
1	9 (18.0)	1 (10.0)	0.021
2	34 (68.0)	5 (50.0)	
3	7 (14.0)	4 (40.0)	
FIGO stage			
III	33 (66.0)	5 (50.0)	0.276
IV	17 (34.0)	5 (50.0)	

Table 2 presents the univariable logistic regression analysis of factors associated with postoperative complications. Age was significantly associated with postoperative complications, with each increase in age associated with higher odds of complications (OR 1.06, 95% CI: 1.00–1.12; $p=0.046$). Similarly, longer operation time was associated with increased odds of complications (OR 1.01, 95% CI: 1.00–1.02; $p=0.031$), while higher albumin levels were associated with lower odds (OR 0.87, 95% CI: 0.76–0.98; $p=0.026$). Among surgical factors, bowel surgery was significantly associated with postoperative complications (OR 4.56, 95% CI: 1.32–16.74; $p=0.016$), as were perioperative blood transfusion (OR 4.15, 95% CI: 1.18–15.72; $p=0.027$), postoperative blood transfusion (OR 3.76, 95% CI: 1.07–13.89; $p=0.039$), and anterior peritonectomy (OR 4.10, 95% CI: 1.09–15.88; $p=0.037$). ASA 3–4 also

showed higher odds of complications, although this did not reach statistical significance (OR 3.48, 95% CI: 0.91–14.83; $p=0.071$). BMI, hemoglobin, white blood cell count, platelet count, lymphocyte count, neutrophil count, CA125, tumor size, menopause, diabetes mellitus, hypertension, previous surgery, surgery type, HIPEC, ascites, suboptimal cytoreduction, pleural effusion, omental cake, peritoneal carcinomatosis, pelvic or diaphragmatic peritonectomy, Aletti scores, and FIGO stage IV were not significantly associated with postoperative complications ($p>0.05$). Overall, the univariable analysis identified older age, longer operative duration, lower albumin, bowel surgery, perioperative and postoperative transfusion, and anterior peritonectomy as significant factors associated with postoperative morbidity.

Table 2: Univariable logistic regression for postoperative complications

Variable	OR (95% CI)	p-value
Age (years)	1.06 (1.00–1.12)	0.046
BMI (kg/m ²)	0.91 (0.80–1.04)	0.172
Operation time (min)	1.01 (1.00–1.02)	0.031
Hemoglobin (g/dL)	0.78 (0.48–1.24)	0.289
White blood cell count ($\times 10^9/L$)	1.12 (0.89–1.46)	0.318
Platelet count ($\times 10^9/L$)	1.00 (0.99–1.01)	0.427
Lymphocyte count ($\times 10^9/L$)	0.71 (0.30–1.54)	0.395
Neutrophil count ($\times 10^9/L$)	1.18 (0.91–1.57)	0.201
Albumin (g/L)	0.87 (0.76–0.98)	0.026
CA125 (U/ml)	1.00 (1.00–1.01)	0.083
Tumor size (cm)	1.09 (0.94–1.28)	0.254
Menopause	2.25 (0.42–15.72)	0.351

Diabetes mellitus	1.52 (0.38–5.87)	0.541
Hypertension	1.94 (0.54–7.11)	0.312
Previous surgery	1.08 (0.31–3.45)	0.901
Surgery type (IDS)	0.84 (0.23–2.83)	0.779
ASA 3–4	3.48 (0.91–14.83)	0.071
HIPEC	1.29 (0.15–10.91)	0.817
Ascites	2.67 (0.69–10.64)	0.146
Bowel surgery	4.56 (1.32–16.74)	0.016
Suboptimal cytoreduction	3.92 (0.63–22.81)	0.118
Perioperative blood transfusion	4.15 (1.18–15.72)	0.027
Postoperative blood transfusion	3.76 (1.07–13.89)	0.039
Pleural effusion	1.95 (0.48–7.31)	0.341
Omental cake	1.56 (0.42–5.84)	0.501
Peritoneal carcinomatosis	1.32 (0.36–5.18)	0.671
Anterior peritonectomy	4.10 (1.09–15.88)	0.037
Pelvic peritonectomy	2.67 (0.71–10.19)	0.148
Diaphragmatic peritonectomy	2.21 (0.57–8.76)	0.254
Aletti score 2	1.32 (0.21–8.44)	0.768
Aletti score 3	4.94 (0.76–32.18)	0.098
FIGO stage IV	1.94 (0.53–7.16)	0.316

Table 3 presents the multivariable logistic regression analysis of factors associated with postoperative complications. Among the variables evaluated, perioperative blood transfusion was the only factor that showed a statistically significant association with postoperative complications, with an OR of 3.86 (95% CI: 1.06–14.72; $p=0.041$), indicating higher odds of postoperative complications among patients who received perioperative transfusion. Bowel surgery showed an elevated odds estimate (OR 2.41, 95% CI: 0.72–8.46), but the association was not statistically significant ($p=0.154$). Similarly,

postoperative blood transfusion (OR 2.28, 95% CI: 0.64–8.91; $p=0.204$), anterior peritonectomy (OR 2.74, 95% CI: 0.70–10.83; $p=0.147$), age (OR 1.04, 95% CI: 0.98–1.11; $p=0.181$), albumin (OR 0.89, 95% CI: 0.77–1.03; $p=0.116$), and ASA grade 3–4 (OR 2.36, 95% CI: 0.62–9.43; $p=0.208$) were not significantly associated with postoperative complications. Overall, after adjustment for the variables included in the model, perioperative blood transfusion emerged as the only statistically significant independent factor associated with postoperative morbidity.

Table 3: Multivariable logistic regression for postoperative complications

Variable	OR (95% CI)	p-value
Bowel surgery	2.41 (0.72–8.46)	0.154
Perioperative blood transfusion	3.86 (1.06–14.72)	0.041
Postoperative blood transfusion	2.28 (0.64–8.91)	0.204
Anterior peritonectomy	2.74 (0.70–10.83)	0.147
Age	1.04 (0.98–1.11)	0.181
Albumin	0.89 (0.77–1.03)	0.116
ASA 3–4	2.36 (0.62–9.43)	0.208

Table 4 summarizes the major postoperative complications classified as Clavien–Dindo grade $\geq$ III. A total of 10 major complications were documented. The most frequent complication was intra-abdominal abscess, classified as grade IIIa, occurring in 2 (20.0%) patients. Other complications occurred in 1 (10.0%) patient each, including intra-abdominal bleeding requiring intervention (IIIb), anastomotic leak (IIIb), intestinal perforation (IIIb), relaparotomy for fascial

dehiscence (IIIb), pulmonary embolism requiring ICU admission (IVa), acute kidney injury (IVa), and severe wound infection requiring intervention (IIIa). In addition, one patient (10.0%) experienced 30-day mortality, classified as Clavien–Dindo grade V. Overall, the complications included gastrointestinal, intra-abdominal, wound, thromboembolic, and renal events, with several requiring invasive intervention or intensive care.

Table 4: Major postoperative complications (Clavien–Dindo $\geq$ III)		
Complication type	Clavien–Dindo grade	n (%)
Intra-abdominal bleeding requiring intervention	IIIb	1 (10.0)
Anastomotic leak	IIIb	1 (10.0)
Intra-abdominal abscess	IIIa	2 (20.0)
Intestinal perforation	IIIb	1 (10.0)
Relaparotomy for fascial dehiscence	IIIb	1 (10.0)
Pulmonary embolism requiring ICU admission	IVa	1 (10.0)
Acute kidney injury	IVa	1 (10.0)
Severe wound infection requiring intervention	IIIa	1 (10.0)
30-day mortality	V	1 (10.0)

Table 5 compares the clinical and laboratory characteristics of patients receiving early chemotherapy (≤ 6 weeks; $n=36$) and delayed chemotherapy (>6 weeks; $n=24$). The median age was 58.0 years [51.0–64.0] in the early group and 62.0 years [53.0–69.0] in the delayed group, with no significant difference ($p=0.192$). Similarly, BMI was comparable between the groups (27.1 [24.4–30.2] vs 26.4 [23.8–30.7] kg/m^2 , $p=0.638$). However, the delayed chemotherapy group had a significantly longer median operation time (270 [215–335] vs 230 [185–285] minutes, $p=0.032$) and longer hospital stay (11 [8–

15] vs 8 [7–10] days, $p=0.008$). Among laboratory parameters, albumin levels were significantly lower in the delayed group (39 [35–43] vs 42 [39–45] g/L, $p=0.041$). No significant differences were observed in hemoglobin, white blood cell count, platelet count, lymphocyte count, neutrophil count, CA125 levels, or tumor size between the two groups (all $p>0.05$). Overall, delayed chemotherapy was characterized by longer operative duration, prolonged hospitalization, and lower albumin levels, while the remaining clinical and laboratory parameters were broadly comparable between the groups.

Table 5: Comparison of clinical and laboratory characteristics between early and delayed chemotherapy groups			
Variable	Early (≤ 6 weeks) ($n=36$)	Delayed (>6 weeks) ($n=24$)	p-value
Age (years)	58.0 [51.0–64.0]	62.0 [53.0–69.0]	0.192
BMI (kg/m^2)	27.1 [24.4–30.2]	26.4 [23.8–30.7]	0.638
Operation time (min)	230 [185–285]	270 [215–335]	0.032
Hospital stay (days)	8 [7–10]	11 [8–15]	0.008
Hemoglobin (g/dL)	11.3 [10.4–12.1]	11.0 [9.9–12.0]	0.341
White blood cell count ($\times 10^9/\text{L}$)	6.3 [5.0–7.8]	6.9 [5.4–8.7]	0.286
Platelet count ($\times 10^9/\text{L}$)	260 [211–318]	272 [203–335]	0.512
Lymphocyte count ($\times 10^9/\text{L}$)	1.8 [1.3–2.3]	1.7 [1.2–2.2]	0.726
Neutrophil count ($\times 10^9/\text{L}$)	3.5 [2.6–4.9]	4.1 [3.0–5.3]	0.177
Albumin (g/L)	42 [39–45]	39 [35–43]	0.041
CA125 (U/ml)	62 [23–220]	105 [31–410]	0.184
Tumor size (cm)	5.0 [3.0–9.0]	5.5 [3.0–10.0]	0.497

Table 6 compares categorical clinical and surgical characteristics between patients receiving early chemotherapy (≤ 6 weeks; $n=36$) and delayed chemotherapy (>6 weeks; $n=24$). Postoperative complications were significantly more frequent in the delayed chemotherapy group than in the early group (29.2% vs 8.3%, $p=0.047$). Similarly, the distribution of Aletti risk scores differed significantly between groups ($p=0.039$), with a higher proportion of patients having a high-risk score in the delayed group (29.2%) compared with the early group (11.1%). Bowel surgery was also significantly more common among patients receiving delayed chemotherapy (33.3% vs 16.7%, $p=0.041$). In contrast, no significant differences were observed in menopause status, parity, diabetes mellitus, hypertension, previous

surgery, surgery type, ASA score, FIGO stage, HIPEC, ascites, perioperative blood transfusion, postoperative blood transfusion, ICU admission, suboptimal cytoreduction, pleural effusion, omental cake, peritoneal carcinomatosis, anterior peritonectomy, pelvic peritonectomy, or diaphragmatic peritonectomy (all $p>0.05$). Although IDS was more frequent in the early group than the delayed group (72.2% vs 50.0%, $p=0.064$), and ASA 3–4 status was more common in the delayed group (58.3% vs 36.1%, $p=0.082$), these differences did not reach statistical significance. Overall, delayed chemotherapy was significantly associated with a higher occurrence of postoperative complications, higher Aletti risk category, and greater frequency of bowel surgery.

Table 6: Comparison of categorical clinical and surgical characteristics between early and delayed chemotherapy groups			
Variable	Early (≤ 6 weeks) (n=36)	Delayed (> 6 weeks) (n=24)	p-value
Complication (Yes)	3 (8.3)	7 (29.2)	0.047
Menopause (Yes)	29 (80.6)	20 (83.3)	0.768
Parity			
No	3 (8.3)	1 (4.2)	0.612
Yes	33 (91.7)	23 (95.8)	
Diabetes mellitus	8 (22.2)	6 (25.0)	0.802
Hypertension	12 (33.3)	10 (41.7)	0.513
Previous surgery			
None	27 (75.0)	17 (70.8)	0.719
Pfannenstiel	7 (19.4)	5 (20.8)	
Midline laparotomy	2 (5.6)	2 (8.3)	
Surgery type			
IDS	26 (72.2)	12 (50.0)	0.064
PDS	10 (27.8)	12 (50.0)	
ASA score			
ASA 1–2	23 (63.9)	10 (41.7)	0.082
ASA 3–4	13 (36.1)	14 (58.3)	
Aletti score			
Low	8 (22.2)	2 (8.3)	0.039
Intermediate	24 (66.7)	15 (62.5)	
High	4 (11.1)	7 (29.2)	
FIGO stage			
III	24 (66.7)	14 (58.3)	0.258
IV	12 (33.3)	10 (41.7)	
HIPEC	3 (8.3)	2 (8.3)	1
Ascites	7 (19.4)	7 (29.2)	0.386
Bowel surgery			
No	30 (83.3)	16 (66.7)	0.041
Yes	6 (16.7)	8 (33.3)	
Perioperative blood transfusion	13 (36.1)	12 (50.0)	0.292
Postoperative blood transfusion	12 (33.3)	14 (58.3)	0.061
ICU admission	7 (19.4)	9 (37.5)	0.128
Suboptimal cytoreduction	2 (5.6)	3 (12.5)	0.391
Pleural effusion	6 (16.7)	6 (25.0)	0.436
Omental cake	24 (66.7)	13 (54.2)	0.326
Peritoneal carcinomatosis	25 (69.4)	14 (58.3)	0.375
Anterior peritonectomy	7 (19.4)	4 (16.7)	0.789
Pelvic peritonectomy	9 (25.0)	5 (20.8)	0.703
Diaphragmatic peritonectomy	8 (22.2)	6 (25.0)	0.802

Discussion

In the present study of 60 patients undergoing cytoreductive surgery for advanced-stage epithelial ovarian cancer, postoperative complications were seen in 10 patients, with the complication burden being dominated by clinically significant Clavien–Dindo grade III or higher complications. Comparative analysis showed that older age, length of surgery, low serum albumin level, high ASA grade, bowel surgery, anterior peritonectomy, and transfusion during and after surgery were risk factors for postoperative morbidity. Perioperative blood transfusion was the only independent risk factor identified, and patients who received transfusion were about four times more likely to develop

postoperative complications (adjusted OR 3.86, 95% CI 1.06–14.72; $p=0.041$). These results may be interpreted as evidence for the theory that the postoperative morbidity following surgery for advanced ovarian cancer is greatly determined by the physiological reserve and the amount of the operation, and not exclusively on the characteristics of the tumor.”

The relationships between surgical complexity and morbidity rate post-surgery noted in this study are similar to what has been noted in literature. Bowel surgery was performed in 50.0% of patients with complications and 18.0% of patients without complications ($p=0.006$), and anterior peritonectomy was performed in 40.0% of patients with complications and 14.0% of patients without complications

($p=0.041$). There was also longer operating time for those who had complications (300 vs 235 minutes, $p=0.018$). Castro et al. also showed that the amount of blood loss during surgery and the patient's status before surgery were factors affecting postoperative morbidity. Of 83 women, 53.5% presented with complications after primary debulking surgery and 67.5% after interval debulking surgery, but the difference between the two surgical procedures was not significant ($p=0.192$). Importantly, comorbidities alone were responsible for an increased risk for complications (OR 5.466), whereas an estimated blood loss > 300 mL was responsible for a significantly increased risk (OR 14.407). This is consistent with our observation that perioperative transfusion, which could be considered as a proxy for significant blood loss and stress during surgery, was the strongest independent determinant of morbidity (adjusted OR 3.86). Castro et al also reported that whether the type of cytoreductive surgery, per se, was the cause of the complication was not statistically different, which is consistent with our finding that there was no difference between primary versus interval debulking in the presence or absence of complications. [10]

Preop Physiological Status is further highlighted by the prospective RISC-GYN study. Inci and others analysed 106 women, who underwent maximal cytoreductive surgery, and found grade $\geq$ IIIb postoperative complications in 19 patients (17.9%) and one postoperative death. They performed a multivariable analysis, which showed that ECOG performance status >1 (OR 13.34), BMI >25 kg/m² (OR 10.48), intraoperative use of norepinephrine (OR 4.69), and intraoperative use of high FFP use (OR 4.11) were significant risk factors for severe complications. By contrast, our study showed that older age and ASA 3–4 status were associated with complications in unadjusted analysis, and that lower albumin was independently associated with increased risk in unadjusted analysis (OR 0.87). This discrepancy in BMI results could be due to the limited size of our cohort and to varying definitions of nutritional and functional risk in other studies. However, both studies highlight the need to recognise vulnerable patients prior to wider cytoreductive surgery. [11]

This is confirmed by the study of Cham et al., the risk-calculator study of 7,029 women undergoing surgery for ovarian, fallopian-tube, or primary peritoneal cancer. Among the strongest risk factors for adverse perioperative outcomes were advanced age, higher ASA status, and multiple extended surgical procedures, the authors found. These observations are consistent with our results, which demonstrated that patients who experienced complications were older, more likely to have ASA 3–4 status and were more likely to receive bowel surgery and anterior peritonectomy. But in our multivariable model, these were not independent after adjusting for transfusion, and some of the apparent effects of surgical

complexity and patient frailty may be due to the amount of blood loss during surgery and the transfusion requirements. [12]

It is significant how severe complications can be in our cohort. The most common major complication was intra-abdominal abscess, with other complications including anastomotic leak, intestinal perforation, intra-abdominal bleeding, acute kidney injury, severe wound infection and pulmonary embolism. One patient died within 30 days. This is clinically relevant as the Clavien–Dindo system reflects the intensity of the therapy and the impact of post-operative events, not just their incidence. Bolliger et al. highlighted the importance of standardized Clavien–Dindo classification to objectively report and compare surgical complications. As a result, our complication profile illustrates that complications associated with extensive ovarian cancer surgery can encompass multiple organ systems and can be associated with significant therapeutic intervention, prolonged recovery and even death [13].

Another significant finding is the link between time of chemotherapy and postoperative recovery. In our cohort, chemotherapy beyond 6 weeks was significantly correlated with a higher complication rate compared to chemotherapy within 6 weeks (29.2% versus 8.3%, $p=0.047$), and delayed chemotherapy was also correlated with longer hospitalization, longer operation time, lower albumin and more bowel surgery. These findings are similar to those of Castro et al., who used a delay of 42 days for chemotherapy after surgery as a cutoff and reported that the postoperative complications were significantly associated with the delay of chemotherapy after surgery. Their independent predictors of chemotherapy delay included hypertension, BMI >30 kg/m², reoperation, and postoperative fever [10]. Therefore, we believe that we have demonstrated that rapid postoperative recovery is clinically important since patients with higher operative burden and postoperative morbidity were more likely to have delayed chemotherapy.

Liu et al. [14] provides further support for the prognostic significance of timing of treatment in their dose-response meta-analysis of 14 studies including 59,569 patients with ovarian cancer. The longest interval was associated with poorer overall survival (HR 1.18, 95% CI 1.06–1.32) and each additional week of delay was associated with a 4% increase in the hazard of death (HR 1.04, 95% CI 1.00–1.09) compared with the shortest interval. Joneborg et al. also emphasized the significance of postoperative morbidity after large upper abdominal surgery due to the fact that it prolongs the time to chemotherapy and morbidity. Median time to chemotherapy (TTC) was 43 days in Rocher et al.'s study of 233 patients, and, in patients with advanced stage, overall survival (OS) was significantly poorer with a TTC > 8 weeks (59.3 versus 70.5 months, $p=0.04$), but not with a

TTC > 6 weeks [16]. These results offer perspective on the six-week threshold as clinically relevant and further indicate that the impact of delays of treatment may be more noticeable when treatment is delayed longer.

Lastly, the conclusions to be drawn from our results on PDS and IDS must be viewed with care. IDS occurred more frequently overall and seemed to allow earlier chemotherapy in our patient population, but surgery itself did not seem to be an important predictor of complications after surgery. This is consistent with Castro et al. who reported that there was no significant difference in complication rates between PDS and IDS. In a similar fashion, the SCORPION randomized trial of 171 patients found a 25.9% incidence of major postoperative complications after PDS versus 7.6% after neoadjuvant chemotherapy plus surgery, with the median progression-free survival being 15 months versus 14 months, respectively, and the overall survival 41 months versus 43 months, respectively. In contrast, Lim et al., [17] showed complete gross resection in 66% versus 79% of PDS and neoadjuvant chemotherapy patients respectively and median PFS of 20 months versus 15 months in 279 patients with bulky stage IIIC–IV disease with estimated median OS of >70 months versus 70 months respectively. All of these studies suggest that treatment choice should be tailored to the extent of disease, patient fitness, expected complexity of surgery, and the likelihood of complete cytoreduction. Perioperative transfusion was the strongest independent predictor in our cohort, highlighting the importance of reducing blood loss and blood transfusion requirements, especially for minimizing morbidity and for timely systemic therapy post-surgery.

Conclusion

The present study concludes that postoperative morbidity following cytoreductive surgery for advanced-stage epithelial ovarian cancer is influenced by a combination of patient-related, nutritional, and operative factors. On initial analysis older age, lower albumin, more surgically complex, higher ASA, bowel surgery, anterior peritonectomy and perioperative blood transfusion were associated with higher postoperative morbidity, and only the transfusion of blood during surgery remained an independent risk factor of postoperative morbidity after multivariable analysis. Complications of particular significance were intra-abdominal infective and surgical events, anastomotic and intestinal complications, thromboembolic and renal events, severe wound infection and postoperative mortality, which showed the possibility of the severe morbidity that can follow extensive cytoreductive procedures. Also, delayed start of chemotherapy was linked with higher complication rates as well as higher surgical complexity, longer hospitalisation and less favourable perioperative features. These findings highlight the need for

thorough pre-operative risk assessment, nutritional and medical optimisation, meticulous surgical planning, judicious blood-conserving strategies and close post-operative monitoring to minimise morbidity and ensure timely recovery to start the adjuvant chemotherapy.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA: a cancer journal for clinicians*. 2020 Jan;70(1):7-30.
2. Colombo N, Sessa C, du Bois A, Ledermann J, McCluggage WG, McNeish I, Morice P, Pignata S, Ray-Coquard I, Vergote I, Baert T. ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. *Annals of oncology*. 2019 May 1;30(5):672-705.
3. Tseng JH, Cowan RA, Zhou Q, Iasonos A, Byrne M, Polcino T, Polen-De C, Gardner GJ, Sonoda Y, Zivanovic O, Abu-Rustum NR. Continuous improvement in primary debulking surgery for advanced ovarian cancer: do increased complete gross resection rates independently lead to increased progression-free and overall survival? *Gynecologic oncology*. 2018 Oct 1;151(1):24-31.
4. Cham S, Chen L, Clair CM, Hou JY, Tergas AI, Melamed A, Ananth CV, Neugut AI, Hershman DL, Wright JD. Development and validation of a risk-calculator for adverse perioperative outcomes for women with ovarian cancer. *American journal of obstetrics and gynecology*. 2019 Jun 1;220(6):571-e1.
5. Colombo N, Sessa C, du Bois A, Ledermann J, McCluggage WG, McNeish I, Morice P, Pignata S, Ray-Coquard I, Vergote I, Baert T. ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. *Annals of oncology*. 2019 May 1;30(5):672-705.
6. Fagotti A, Ferrandina G, Vizzielli G, Fanfani F, Gallotta V, Chiantera V, Costantini B, Margariti PA, Alletti SG, Cosentino F, Tortorella L. Phase III randomised clinical trial comparing primary surgery versus neoadjuvant chemotherapy in advanced epithelial ovarian cancer with high tumour load (SCORPION trial): Final analysis of peri-operative outcome. *European journal of cancer*. 2016 May 1;59:22-33.
7. Tewari KS, Java JJ, Eskander RN, Monk BJ, Burger RA. Early initiation of chemotherapy following complete resection of advanced ovarian cancer associated with improved survival: NRG Oncology/Gynecologic Oncology Group study. *Annals of Oncology*. 2016 Jan 1;27(1):114-21.

8. Timmermans M, Van Der Aa MA, Lalisang RI, Witteveen PO, Van de Vijver KK, Kruitwagen RF, Sonke GS. Interval between debulking surgery and adjuvant chemotherapy is associated with overall survival in patients with advanced ovarian cancer. *Gynecologic oncology*. 2018 Sep 1;150(3):446-50.
9. Tewarie NB, Van Driel WJ, van Ham MA, Wouters MW, Kruitwagen RF, Kruse AJ, Yigit R, van der Aa M, Mens JW, Stam TC, Diepstraten J. Postoperative outcomes of primary and interval cytoreductive surgery for advanced ovarian cancer registered in the Dutch Gynecological Oncology Audit (DGOA). *Gynecologic Oncology*. 2021 Aug 1;162(2):331-8.
10. Castro BG, Dos Reis R, Cintra GF, de Assuncao Sousa MM, de Andrade Vieira M, da Cunha Andrade CE. Predictive factors for surgical morbidities and adjuvant chemotherapy delay for advanced ovarian cancer patients treated by primary debulking surgery or interval debulking surgery. *International Journal of Gynecological Cancer*. 2018 Oct 1;28(8):1520-8.
11. Inci MG, Rasch J, Woopen H, Mueller K, Richter R, Schouli J. ECOG and BMI as preoperative risk factors for severe postoperative complications in ovarian cancer patients: results of a prospective study (RISC-GYN—trial). *Archives of Gynecology and Obstetrics*. 2021 Nov;304(5):1323-33.
12. Cham S, Chen L, Clair CM, Hou JY, Tergas AI, Melamed A, Ananth CV, Neugut AI, Hershman DL, Wright JD. Development and validation of a risk-calculator for adverse perioperative outcomes for women with ovarian cancer. *American journal of obstetrics and gynecology*. 2019 Jun 1;220(6):571-e1.
13. Bolliger M, Kroehnert JA, Molineus F, Kandoler D, Schindl M, Riss P. Experiences with the standardized classification of surgical complications (Clavien-Dindo) in general surgery patients. *European Surgery*. 2018 Dec;50(6):256-61.
14. Liu Y, Zhang T, Wu Q, Jiao Y, Gong T, Ma X, Li D. Relationship between initiation time of adjuvant chemotherapy and survival in ovarian cancer patients: a dose-response meta-analysis of cohort studies. *Scientific reports*. 2017 Aug 25;7(1):9461.
15. Joneborg U, Palsdottir K, Farm E, Johansson H, Salehi S. Time-interval to adjuvant chemotherapy and postoperative management after upper abdominal surgical procedures in advanced ovarian cancer. *European Journal of Surgical Oncology*. 2021 Feb 1;47(2):353-9.
16. Rocher G, Gaillard T, Uzan C, Collinet P, Bolze PA, Ballester M, Bendifallah S, Ouldamer L, Touboul C, Huchon C, Lavoue V. Does time-to-chemotherapy after primary complete macroscopic cytoreductive surgery influence prognosis for patients with epithelial ovarian cancer? A study of the FRANCOGYN group. *Journal of Clinical Medicine*. 2021 Mar 4;10(5):1058.
17. Lim MC, Yoo HJ, Song YJ, Seo SS, Kang S, Kim SH, Yoo CW, Park SY. Survival outcomes after extensive cytoreductive surgery and selective neoadjuvant chemotherapy according to institutional criteria in bulky stage IIIC and IV epithelial ovarian cancer. *J Gynecol Oncol*. 2017 Jul 1;28(4):e48.