ECOG and BMI as preoperative risk factors for severe postoperative complications in ovarian cancer patients: results of a prospective study (RISC-GYN—trial)

Melisa Guelhan Inci1 · Julia Rasch1 · Hannah Woopen1 · Kristina Mueller1 · Rolf Richter1 · Jalid Sehouli1

Received: 11 January 2021 / Accepted: 2 June 2021 / Published online: 24 June 2021
© The Author(s) 2021

Abstract

Background Accompanying co-morbidities in patients with ovarian cancer are of major relevance for scheduling debulking surgery, especially in the anesthesiological consultations. Aim of this study was to evaluate the impact of co-morbidities and patient characteristics on postoperative complications.

Methods Patients undergoing maximal cytoreductive surgery were prospectively enrolled from October 2015 to January 2017. Various variables were recorded, such as the Charlson comorbidity index, Eastern cooperative oncology group scale of performance status (ECOG PS) and the American society of anesthesiologists physical status classification system (ASA PS). Surgical complications were graded using the Clavien–Dindo criteria. Logistic regression models were used to analyze risk factors for severe postoperative complications.

Results Of 106 enrolled patients, 19 (17.9%) developed severe postoperative complications grade ≥ IIIb according to Clavien–Dindo criteria. In the multivariable regression analysis impaired (ECOG PS) > 1 (odds ratio OR) 13.34, 95% confidence interval (CI) 1.74–102.30, \( p = 0.01 \), body mass index (BMI) > 25 kg/m² (OR 10.48, 95% CI 2.38–46.02, \( p = 0.002 \)) along with the use of intraoperative norepinephrine > 0.11 µg/kg/min (OR 4.69, 95% CI 1.13–19.46, \( p = 0.03 \)) and intraoperative fresh frozen plasma (FFP) > 17 units (OR 4.11, 95% CI 1.12–15.14, \( p = 0.03 \)) appeared as significant predictors of severe postoperative complications.

Conclusion We demonstrated that neither the presence of a certain comorbidity nor the summation of the co-morbidities were associated with adverse outcome. Patient characteristics, such as ECOG PS > 1 and obesity (BMI > 25 kg/m²), are highly predictive factors for severe postoperative complications. The analysis of intraoperative data showed that the need for more than > 0.11 µg/kg/min of norepinephrine and transfusions of FFPs more than 17 units were strongly associated with severe postoperative complications.

Keywords Ovarian cancer · Performance status · Body mass index · Comorbidity · Gynecology · Surgery · Postoperative complications

Background

Complete cytoreduction is one of the main prognostic factors for patients with ovarian cancer [1–3]. To achieve complete macroscopic tumor resection, extensive multi-visceral procedures are performed [4]. Severe complications can be the result of complex procedures. These complications can result in prolonged recovery periods and delays in the initiation of adjuvant therapy with consequent worsened overall outcome [4, 5]. When alternate strategies such as neoadjuvant chemotherapy are discussed, the individual evaluation of patients is crucial [6–8]. Accompanying co-morbidities in patients with ovarian cancer are of great importance in the...
pre-surgical anesthesiological consultation for the debulking operation [9]. Also, elements, such as age, body mass index (BMI), American society of anesthesiologists physical status classification system (ASA PS), preoperative albumin, Fédération Internationale de Gynécologie et d’Obstétrique (FIGO) stage, and surgical complexity, were found to hold a significant level of predictive ability [10–14].

The aim of this study was to evaluate potential predictive markers for severe postoperative complications in ovarian cancer surgery, such as co-morbidities and further clinical characteristics.

Methods

Study design and patient population

This analysis is part of the prospective study named “RISC-GYN—trial”. The study was designed to explore predictive markers for severe postoperative complications in gynecologic cancer patients. Out of this cohort with gynecologic cancer patients, we selected 155 ovarian cancer patients as the largest entity within the RISC-GYN—trial. We later excluded patients with recurrent disease. See Fig. 1 for consort diagram. Ethical approval was received from the local Ethics Committee (Charité—Universitätsmedizin Berlin) with the approval ID EA2/122/15. Data have been collected prospectively from October 2015 to January 2017. All surgeries were performed by specialized gynecologic oncology surgeons. Inclusion criteria were age above 18 years, histologically confirmed malignancy or a high suspicion of a gynecologic malignancy arising from imaging and laboratory results, and surgery with an expected minimal duration of 60 min. Written consent was required from all patients. Assessment consisted of a thorough medical history of all patients including co-morbidities and medications, as well as height and weight. Single-item questions were asked concerning sociodemographic, lifestyle and physical activity. Laboratory values were derived from preoperative routinely performed blood tests.

The Charlson comorbidity index was calculated for each patient as previously published by Charlson et al. [15]. By adding one further point per decade, starting at 50–59, the age-adjusted Charlson comorbidity index was calculated [16]. To define each patient’s performance status, ECOG PS and ASA PS were recorded by gynecologists and anesthesiologists prior to surgery [17–19].

Information on performed operative procedures, perioperative anesthesiologic parameters and tumor dissemination pattern was documented intraoperatively. The intraoperative mapping of ovarian cancer (IMO) was applied for exact tumor documentation [20].

Each patient was visited systematically in a daily schedule until the end of their hospital stay and was followed up via phone after 3 months post surgery. Our primary outcome of interest was 30-day postoperative complications Clavien–Dindo classification grade IIIb, IV and V. Clavien–Dindo classification grade IIIb complications require an intervention under general anesthesia [21]. See Supplementary 1 for detailed explanation. According to the severity of their postoperative complications, patients were divided into two cohorts: non- and mild postoperative complications (grade 0–IIIa) and severe postoperative complications (grade IIIb–V).

Statistical analysis

Where appropriate the Fisher’s exact test for dichotomous variables, Kendall’s tau b for ordinal variables, the chi test for nominal variables and Kruskal–Wallis test or Mann–Whitney test for continuous variables were performed to evaluate comparisons between groups.

To assess the predictive accuracy of continuous variables for distinguishing patients with severe postoperative complications from those without severe postoperative
complications and to determine cut-offs, receiver-operator characteristics (ROC) curve analyses were used (see Fig. 2). Logistic regression analysis was performed to obtain crude and adjusted odds ratios (ORs) with corresponding 95% confidence interval (95% CI). Multivariable logistic regression analyses were executed stepwise with $p_{in} = 0.05$ and $p_{out} = 0.10$. Excluded from the multivariable analyses were cases with missing values. For statistical analysis, IBM® SPSS® Statistics 25 (SPSS Inc. an IBM Company, Chicago, IL, USA) was used and statistical significance was defined as $p < 0.05$ without alteration for multiple comparisons.

**Results**

A total of 106 women undergoing surgery for ovarian cancer were enrolled in the study. Baseline characteristics of the study cohort are presented in Table 1.

**Fig. 2** ROC analysis to define cut-offs for **A** BMI, **B** ECOG PS, **C** number of transfused FFP and, **D** highest intraoperative need for norepinephrine for predicting severe postoperative complications.
Overall, 19 patients (17.9%) experienced complications Clavien–Dindo Classification grade ≥ IIIb and one of them (0.9%) died within 30 days of surgery. The most common complications were urinary tract infections (n = 14, 13%), postoperative pleural effusions (n = 31, 29%), anastomotic insufficiency (n = 9, 8%), wound dehiscence (n = 5, 4%), peritonitis (n = 5, 4%), and thromboembolic events (n = 5, 4%). Table 2 shows the complications that occurred. The most common co-morbidities were arterial hypertension (n = 34, 32%), polyneuropathy (n = 23, 22%), chronic pulmonary disease (n = 10, 9%) and diabetes mellitus type I and type II (n = 9, 8%). Cardiovascular disease (n = 35, 37%) was defined as current or condition after myocardial infarction, heart failure, peripheral vascular disease, cerebrovascular disease, cardiac arrhythmias and atrial fibrillation. See Table 3 for further details of the distribution of co-morbidities.

The patients with serious postoperative complications had significantly more co-morbidities (Charlson comorbidity

**Table 1** Baseline Characteristics

| Characteristics                  | Total n = 106 | Clavien–Dindo classification grade 0–IIIa n = 87 | Clavien–Dindo classification grade ≥ IIIb n = 19 | p value |
|----------------------------------|--------------|-----------------------------------------------|-----------------------------------------------|---------|
| Median age in years              | 57 (18–87)   | 55 (18–86)                                    | 63 (31–87)                                    | 0.2     |
| Age ≥ 65 years                   | 42 (39.6)    | 32 (36.8)                                     | 10 (52.6)                                     | 0.2     |
| Age ≥ 70 years                   | 28 (26.4)    | 21 (24.1)                                     | 7 (36.8)                                      | 0.3     |
| Underweight (BMI < 20 kg/m²)     | 15 (14.2)    | 15 (17.2)                                     | 0                                             | < 0.001 |
| Normal (BMI 20–25 kg/m²)         | 43 (40.6)    | 40 (46.0)                                     | 3 (15.8)                                      |         |
| Overweight (BMI 25–30 kg/m²)     | 28 (26.4)    | 19 (21.8)                                     | 9 (47.4)                                      |         |
| Obese (BMI > 30 kg/m²)           | 20 (18.9)    | 13 (14.9)                                     | 7 (36.8)                                      |         |
| Preoperative albumin < 35.6 g/l  | 15 (15.6)    | 9 (11.5)                                      | 6 (33.3)                                      | 0.02    |
| Preoperative potassium < 3.7 mmol/l | 12 (11.4) | 7 (8.1)                                      | 5 (26.3)                                      | 0.02    |
| Charlson comorbidity index ≥ 1   | 32 (30.2)    | 20 (23.0)                                     | 12 (63.2)                                     | 0.001   |
| Hypertension                     | 34 (32.1)    | 27 (31.0)                                     | 7 (36.8)                                      | 0.6     |
| Diabetes mellitus type I and type II | 9 (8.5)  | 5 (5.7)                                       | 4 (21.1)                                      | 0.03    |
| Polypharmacy (> 5 medications)   | 21 (19.8)    | 13 (14.9)                                     | 8 (42.1)                                      | 0.007   |
| Smoking daily                    | 24 (22.5)    | 21 (24.1)                                     | 3 (15.8)                                      | 0.4     |
| Alcohol consumption daily        | 13 (12.3)    | 11 (12.6)                                     | 2 (10.5)                                      | 0.8     |
| ASA PS > 2                       | 29 (27.6)    | 21 (24.1)                                     | 8 (44.4)                                      | 0.08    |
| ECOG PS > 1                      | 8 (7.5)      | 3 (3.4)                                       | 5 (26.3)                                      | 0.001   |
| FIGO stage                       |              |                                               |                                               | 0.6     |
| I–II                             | 17 (16.2)    | 15 (17.4)                                     | 2 (10.6)                                      | 0.4     |
| III–IV                           | 88 (83.8)    | 71 (82.5)                                     | 17 (89.6)                                     |         |
| High-grade                       | 91 (92.9)    | 75 (92.6)                                     | 16 (94.1)                                     | 0.2     |
| Low-grade                        | 7 (7.1)      | 6 (7.4)                                       | 1 (5.9)                                       |         |
| Neoadjuvant chemotherapy         | 11           | 9                                              | 2                                             | 1.0     |
| Presence of ascites              | 59 (59.0)    | 44 (54.3)                                     | 15 (78.9)                                     | 0.4     |

BMI body mass index, ASA PS American society of anesthesiologists physical status classification system, ECOG PS eastern cooperative oncology group scale of performance status, FIGO fédération internationale de gynécologie et d’obstétrique, CA cancer antigen

**Table 2** Types and frequency of postoperative complications

| Type                           | n (%) |
|--------------------------------|-------|
| Wound dehiscence               | 5 (4.7) |
| Anastomotic insufficiency       | 9 (8.5) |
| Thromboembolic events          | 5 (4.7) |
| Ileus                          | 3 (2.8) |
| Organ failure                  | 1 (0.9) |
| Sepsis                         | 4 (3.8) |
| Peritonitis                    | 5 (4.7) |
| Fistula                        | 1 (0.9) |
| Intestinal perforation         | 2 (1.9) |
| Delir                          | 4 (3.8) |
| Neurological disorder          | 5 (4.7) |
| Postoperative pleural effusions| 31 (29.3) |
| Pneumonia                      | 5 (4.7) |
| Pneumothorax                   | 3 (2.8) |
| Urinary tract infections       | 14 (13.2) |
index ≥ 1; 63 vs. 23%; \( p = 0.001 \), a higher rate of polypharmacy (> 5 medications; 42 vs. 15%; \( p = 0.007 \)), diabetes (21 vs. 6%; \( p = 0.03 \)), compared to patients without or with less severe complications. They showed significantly more often hypokalemia (26 vs. 8%; \( p = 0.02 \)), hypoalbuminemia (33 vs. 12%; \( p = 0.02 \)) and a high level of CA 125 (> 500 U/ml) (28 vs. 7%; \( p = 0.005 \)). Their ECOG PS was more often impaired (26 vs. 3%; \( p = 0.001 \)) as a continuous variable (OR 1.91, 95% CI 0.70–5.19, \( p = 0.2 \)) and age ≥ 70 years (OR 1.83, 95% CI 0.64–5.26, \( p = 0.3 \)) showed no association with severe postoperative complications.

**Table 3** Distribution of co-morbidities according to the Charlson comorbidity index and co-morbidities not included in the Charlson comorbidity index

| Charlson comorbidity index | \( n (\%) \) |
|----------------------------|-------------|
| Diabetes mellitus without end-organ damage | 9 (8.5) |
| Cerebrovascular disease | 2 (1.9) |
| Myocardial infarction | 4 (3.8) |
| Congestive heart failure | 5 (4.7) |
| Peripheral vascular disease | 2 (1.9) |
| Dementia | 0 |
| Chronic pulmonary disease | 10 (9.4) |
| Connective tissue disease | 4 (3.8) |
| Peptic ulcer disease | 3 (2.8) |
| Mild liver disease | 1 (0.9) |
| Diabetes mellitus with end-organ damage | 0 |
| Moderate/severe renal disease | 2 (1.9) |
| Hemiplegia | 0 |
| Solid tumor without metastasis | 0 |
| Leukemia | 0 |
| Lymphoma | 0 |
| Moderate/severe liver disease | 1 (0.9) |
| Metastatic solid tumor | 0 |
| Acquired immune deficiency syndrome | 0 |

**Comorbidities not included in Charlson comorbidity index**

| \( n (\%) \) |
|-------------|
| Hypertension | 34 (32.1) |
| Polyneuropathy | 23 (14.8) |
| Lymphedema | 3 (2.8) |
| Cardiac arrhythmias | 14 (13.2) |
| Atrial fibrillation | 8 (7.5) |

index ≥ 1) was significantly associated with severe postoperative complications (OR 5.74, 95% CI 2.00–16.54, \( p = 0.001 \)). The age-adjusted Charlson comorbidity index showed significance at a cut-off point of ≥ 2 (OR 5.08, 95% CI 1.74–14.83, \( p = 0.003 \)).

Cardiovascular disease (OR 3.79, 95% CI 1.29–11.12, \( p = 0.02 \)) and diabetes (OR 4.37, 95% CI 1.05–18.19, \( p = 0.04 \)), bowel obstruction symptoms (OR 8.00, 95% CI 1.23–51.56, \( p = 0.03 \)) and the simultaneous intake of more than five medications (OR 4.14, 95% CI 1.40–12.25, \( p = 0.01 \)) were significantly related in univariate logistic regression, whereas hypertension was not. Liver disease, chronic pulmonary disease and renal disease did not show correlation to severe postoperative complications. Hypokalemia (< 3.7 mmol/l) (OR 4.03, 95% CI 1.12–14.50, \( p = 0.03 \)), a decreased INR (≤ 0.9) (OR 9.84, 95% CI 1.71–56.68, \( p = 0.01 \)) and hyperbilirubinemia (> 0.46 mg/dl) (OR 3.62, 95% CI 0.98–13.42, \( p = 0.05 \)) were associated with severe postoperative complications.

Overweight patients with a BMI > 25–30 kg/m² were 8 times more likely to develop complications (OR 8.68, 95% CI 2.13–35.46, \( p = 0.003 \)) and obese patients with a BMI

**Analysis of association of preoperative patient-related characteristics and severe postoperative complications (≥ grade IIIb) by Clavien–Dindo classification**

An ASA PS > 2 and ECOG PS > 1 were associated with severe complications (OR 2.51; 95% CI 0.88–7.20; \( p < 0.09 \)) and (OR 10.0; 95% CI 2.15–46.61; \( p = 0.003 \)), respectively.

Univariate logistic regression showed further that an increased number of co-morbidities (Charlson comorbidity index ≥ 1) was significantly associated with severe postoperative complications (OR 5.74, 95% CI 2.00–16.54, \( p = 0.001 \)). The age-adjusted Charlson comorbidity index showed significance at a cut-off point of ≥ 2 (OR 5.08, 95% CI 1.74–14.83, \( p = 0.003 \)).
above 30 kg/m² were up to 9 times more likely to develop severe postoperative complications (OR 9.87, 95% CI 2.24–43.43, \( p = 0.002 \)).

All the preoperative variables were included in the stepwise logistic regression. ECOG PS > 1 (OR 8.87, 95% CI 1.34–58.75, \( p = 0.02 \)) showed the greatest correlation with severe postoperative complications. Overweight and obesity (BMI > 25 kg/m², OR 8.54, 95% CI 1.82–31.37, \( p < 0.005 \)) were highly predictive as well. Furthermore, the Charlson comorbidity index (OR 3.33, 95% CI 1.03–10.81, \( p = 0.05 \)) was an independent predictive parameter. The age-adjusted Charlson comorbidity index and all the assessed co-morbidities lost significance in multivariate analysis. See Table 4 for detailed information of multivariate analysis for preoperative variables.

### Table 4

| Patient demographics | Univariate analysis unadjusted OR (95% CI) | \( p \) value | Multivariate analysis adjusted OR (95% CI) | \( p \) value |
|----------------------|------------------------------------------|--------------|------------------------------------------|--------------|
| Age (continuous variable) | 1.91 (0.70–5.19) | 0.2 | | |
| Age ≥ 70 years | 1.83 (0.64–5.26) | 0.3 | | |
| Alcohol consumption daily | 0.81 (0.17–4.01) | 0.8 | | |
| Smoking daily | 0.59 (0.16–2.22) | 0.4 | | |
| Performance status | | | | |
| ASA PS > 2 | 2.51 (0.8–7.20) | 0.09 | | |
| ECOG PS > 1 | 10.0 (2.15–46.61) | 0.003 | 8.87 (1.34–58.75) | 0.02 |
| Comorbidities | | | | |
| Charlson comorbidity index ≥ 1 | 5.74 (2.00–16.54) | 0.001 | 3.33 (1.03–10.81) | 0.05 |
| Age-adjusted Charlson comorbidity index > 2 | 5.08 (1.74–14.83) | 0.003 | | |
| Polypharmacy (> 5 medications) | 4.14 (1.40–12.25) | 0.01 | | |
| Bowel obstruction symptoms | 8.00 (1.23–51.56) | 0.03 | | |
| Diabetes mellitus type I and II | 4.37 (1.05–18.19) | 0.04 | | |
| Cardiovascular disease | 3.79 (1.29–11.12) | 0.02 | | |
| Renal disease | 1.09 (0.12–10.13) | 1.0 | | |
| Chronic pulmonary disease | 2.14 (0.50–9.18) | 0.3 | | |
| Liver disease | 4.78 (0.29–80.0) | 0.3 | | |
| Hypertension | 1.30 (0.46–3.66) | 0.6 | | |
| Thromboembolic event | 0.86 (0.18–4.15) | 1.0 | | |
| Polyneuropathy | 0.75 (0.90–6.62) | 0.8 | | |
| BMI (kg/m²) categorical | | | | |
| < 20 | 0.00 (0.00–0.00) | 1.00 | | |
| 26–30 overweight | 8.68 (2.13–35.46) | 0.003 | | |
| > 30 obese | 9.87 (2.24–43.43) | 0.002 | 8.54 (1.82–31.37) | 0.005 |
| Laboratory variables | | | | |
| Potassium < 3.7 mmol/l | 4.03 (1.12–14.50) | 0.03 | | |
| INR ≤ 0.9 | 9.84 (1.71–56.68) | 0.01 | | |
| Creatinine > 0.75 mg/dl | 2.01 (0.74–5.47) | 0.17 | | |
| Albumin < 35.6 g/l | 3.83 (1.15–12.74) | 0.03 | | |
| GFR < 81.5 ml/min | 0.43 (0.16–1.17) | 0.1 | | |
| Hemoglobin < 12.25 g/dl | 0.37 (0.99–1.37) | 0.1 | | |
| Sodium < 137 mmol/l | 1.43 (0.35–5.77) | 0.6 | | |
| ALT > 35 U/l | 1.65 (0.39–6.97) | 0.5 | | |
| AST > 35 U/l | 1.34 (0.38–4.74) | 0.7 | | |
| Bilirubin > 0.46 mg/dl | 3.62 (0.98–13.42) | 0.05 | | |

ASA PS American society of anesthesiologists physical status classification system, ECOG PS eastern cooperative oncology group scale of performance status, BMI body mass index, INR international normalized ratio, GFR glomerular filtration rate, ALT alanine transaminase, AST aspartate transaminase
Association of intraoperative data, tumor-related data and severe postoperative complications (≥ grade IIIb) by Clavien–Dindo classification

The surgical procedures of special interest included bowel resection with resection of the large intestine (n = 56, 53%), the small intestine (n = 17, 16%), upper abdominal surgery (n = 36, 34%) and pelvic and/or paraaortic lymphonectomy (n = 77, 72%). In univariate analysis, most of the surgical procedures, prolonged duration of surgery, intraoperative hypothermia (< 36 °C) and most of the tumor-related characteristics did not show significant correlation with complications.

Only the use of more than 0.11 µg/kg/min norepinephrine (OR 3.00, 95% CI 0.99–9.05, p = 0.05), the use of fresh frozen plasma (OR 4.26, 95% CI 1.51–12.04, p = 0.006) and a level of CA 125 > 500 U/ml (OR 2.98, 95% CI 1.04–8.51, p = 0.04) showed significant association.

The intraoperative and tumor-related parameters were also analyzed in a stepwise logistic regression. Only the use of more than 17 intraoperative fresh frozen plasma units (OR 5.93, 95% CI 1.70–20.61, p = 0.005) and the pelvic and/or para-aortic lymphadenectomy (OR 3.43, 95% CI 1.04–11.30, p = 0.04) remained significantly associated with severe postoperative complications.

See Table 5 for further details. See Fig. 2 for the ROC-analysis that was used to define cut-offs for prolonged surgery duration and highest intraoperative need for norepinephrine for predicting severe postoperative complications.

Multivariate analysis of preoperative, intraoperative and tumor-related parameters and severe postoperative complications (≥ grade IIIb) by Clavien–Dindo classification

Ultimately, to all significant factors from the preoperative analysis, the intraoperative and tumor-related parameters were added into stepwise logistic regression. Table 6 shows BMI > 25 kg/m² (OR 10.48, 95% CI 2.38–46.02, p = 0.002), ECOG PS > 1 (OR 13.34, 95% CI 1.74–102.30, p = 0.01), and

Table 5  Univariate analysis and multivariate analysis of intraoperative data and tumor-related characteristics

| Characteristics | n  | %   | Univariate analysis | Multivariate analysis |
|-----------------|----|-----|---------------------|-----------------------|
| Anaesthesiological data | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | p value | n value |
| Surgery duration > 255 min | 76 | 71.7 | 1.60 (0.48–5.28) | 0.4 | 0.4 |
| Norepinephrine > 0.11 µg/kg/min | 56 | 52.8 | 3.00 (0.99–9.05) | 0.05 | 0.05 |
| Intraoperative FFP > 17 | 23 | 21.7 | 4.26 (1.51–12.04) | 0.006 | 5.93 (1.70–20.61) | 0.005 |
| Blood transfusion > 1 | 48 | 45.3 | 2.43 (0.87–6.77) | 0.09 | 0.09 |
| Hypothermia (intraoperative temperature < 36 °C) | 32 | 30.2 | 0.31 (0.06–1.73) | 0.2 | 0.2 |
| Operative data | | | | | |
| Pelvic and/or para-aortic lymphadenectomy | 77 | 72.6 | 2.29 (0.81–6.43) | 0.1 | 3.43 (1.04–11.30) | 0.04 |
| Upper abdominal surgery | 36 | 34.0 | 1.53 (0.56–4.32) | 0.4 | 0.4 |
| Large bowel resection | 56 | 52.8 | 1.83 (0.60–5.55) | 0.3 | 0.3 |
| Small bowel resection | 17 | 16.0 | 0.98 (0.25–3.81) | 1.0 | 1.0 |
| Peritoneal carcinomatosis | 83 | 78.3 | 2.71 (0.58–12.68) | 0.2 | 0.2 |
| Neoadjuvant chemotherapy | 11 | 10.4 | 1.02 (0.20–5.15) | 1.0 | 1.0 |
| Tumor-related characteristics | | | | | |
| No residual disease | 67 | 63.2 | 1.40 (0.51–3.88) | 0.5 | 0.5 |
| Residual disease | 37 | 34.9 | 1.40 (0.51–3.88) | 0.5 | 0.5 |
| FIGO stage | | | | | |
| I | 11 | 10.4 | | | |
| II | 6 | 5.7 | 2.00 (1.00–39.08) | 0.7 | 0.7 |
| III | 65 | 61.3 | 2.26 (0.26–19.42) | 0.5 | 0.5 |
| IV | 23 | 21.7 | 2.78 (0.28–27.21) | 0.4 | 0.4 |
| Low-grade | 7 | 6.6 | | | |
| High-grade | 91 | 85.8 | 1.35 (0.28–6.47) | 0.7 | 0.7 |
| Presence of ascites | 70 | 66.0 | 3.15 (0.96–10.33) | 0.06 | 0.06 |

FFP fresh frozen plasma, FIGO Fédération Internationale de Gynécologie et d’Obstétrique, CA cancer antigen
the use of more than \( > 0.11 \mu g/kg/min \) norepinephrine (OR 4.69, 95% CI 1.13–19.46, \( p = 0.03 \)) and the use of more than 17 intraoperative FFP units (OR 4.11, 95% CI 1.12–15.14, \( p = 0.03 \)) predictive for severe postoperative complications.

### Discussion

Several studies report an association between co-morbidities and clinical outcome but most of them are performed retrospectively and heterogeneous patient populations limit their interpretation [14, 22]. Therefore, we conducted this prospective study in patients with ovarian cancer.

We screened systematically all co-morbidities and several preoperatively assessed patient-related characteristics, as well as intraoperative anaesthesiological, surgical and tumor-related parameters in this prospective study to assess their impact on 30 days’ postoperative complications in ovarian cancer patients. In the first part of the data analysis, we demonstrated that preoperative patient-related characteristics, such as ECOG PS > 1, obesity and the Charlson comorbidity index, are predictive factors for postoperative complications. In the second part, the analysis of intraoperative data showed the performance of lymphadenectomy and the high need for fresh frozen plasma transfusions to be strongly associated with severe postoperative complications.

The combined evaluation of preoperative and intraoperative factors showed ECOG PS > 1, overweight and obesity/a BMI > 25 kg/m\(^2\), high need of intraoperative FFP and norepinephrine are associated with severe postoperative complications.

The age of the patients showed no association with complications, not even for patients above the age of 70 year. Other studies showed that older patients are at increased risk of surgical morbidity, but if they are able to tolerate aggressive surgical management, the benefit was equivalent to that of younger women [23]. In contrast to our results, age and stage were associated with increased risk for 30-day morbidity and mortality in other studies. However, these studies included only advanced-stage ovarian cancer patients and focused on the elderly [24, 25].

Previous studies have identified the ASA PS and ECOG PS as good tools for outcome prediction in cancer patients [3, 10, 23, 26]. Our results suggest that the ECOG PS is more relevant in oncologic surgery than the ASA PS, evaluating how independently a patient can manage everyday life rather than focusing on systemic diseases. Looking further to evaluate co-morbidities and organ dysfunction affecting the surgical outcome, none of the co-morbidities remained an independent predictor for postoperative complications in multivariate analysis. Our findings suggest that even multi-morbid patients do not require less aggressive surgical treatment plans.

Several publications focusing on ovarian cancer showed obesity as a highly predictive factor for postoperative complications [10, 26–32]. Extreme BMIs—both high and low, have been found to be associated with severe postoperative complications [10]. In our study, underweight was not predictive for postoperative complications, whereas obesity remained an independent predictor. This adds to an earlier prospective publication, which found frail patients to be obese rather than underweight and which stated that weight itself might not be a marker for physiologic reserve [13]. These patients often suffer from impaired wound healing and surgeons face more complex conditions in obese patients, as longer surgery duration is required to obtain equivalent surgical results [29, 31]. These findings are particularly important as obesity is becoming increasingly prevalent in our society.

In our analysis of intraoperative data, we intentionally did not group the surgical interventions as other studies did [12]. To examine the effect of each intervention on postoperative complications, we performed the stepwise logistic regression analysis with all surgical interventions of interest and only the lymphadenectomy showed significant correlation. This is in line with prior studies which discussed that patients with macroscopically complete resection did not benefit from systemic lymphadenectomy [33].

In our study, the use of high levels of norepinephrine and FFP correlated significantly with postoperative complications. The effect of vasoactive medication on gastrointestinal oxygen supply and microcirculatory blood flow is controversially discussed in several studies [34–37]. The exact interaction between catecholamines and simultaneously given anesthetics remains uncertain, as there are disparities of drug effect in different species and different gastrointestinal segments and experimental results cannot be extended into the clinical setting yet. However, if the microcirculation in

### Table 6

| Adjusted OR (95% CI) | \( p \) value |
|----------------------|--------------|
| Overweight and obesity (BMI > 25 kg/m\(^2\)) | 10.48 (2.38–46.02) | 0.002 |
| ECOG performance status > 1 | 13.34 (1.74–102.30) | 0.01 |
| Intraoperative fresh frozen plasma > 17 | 4.11 (1.12–15.14) | 0.03 |
| Norepinephrine > 0.11 µg/kg/min | 4.69 (1.13–19.46) | 0.03 |

ECOG PS Eastern cooperative oncology group scale of performance status
the gastrointestinal in the gastrointestinal tract is reduced, this may cause impaired wound healing, especially in the anastomosis region. Similar to the report of other studies, the rate of anastomotic insufficiency in our cohort was 8.5% [38, 39]. Currently, the debate about the efficacy of FFP and its possible impact in cancer surgery is ongoing [40–43]. We assume that both, the need for norepinephrine and for FFP to stabilize hemodynamics during surgery are multi-factorially related and are indicators for poor general condition of the patient.

In this study, we screened all accompanying co-morbidities in patients with ovarian cancer systematically. Neither the summation of the co-morbidities assessed by the Charlson comorbidity index nor the presence of a certain comorbidity was associated with postoperative complications in the multivariate analysis of pre- and intraoperative parameters.

Our findings imply that the patient characteristics, such as ECOG performance status and BMI, could have greater effect on complications than the co-morbidities and the complex surgical interventions themselves.

There is a limitation noted for this study, as we included patients with different tumor stages and analyzed a heterogeneous set of data. As our results are based on regression analysis, we cannot simply state causation, especially as the individual variables are influenced by each other. However, our findings contribute to a clearer picture of patients who will benefit from surgery.

The main strength of our study is, that it is a prospective study which examined predictive factors for postoperative complications as the primary endpoint. Using the Clavien–Dindo classification to grade postoperative complications made our results more objective as well as comparable and reproducible for future research. The homogeneous and very high quality of surgical treatment as well as daily visits of each patient lead to further improvement of reliability and validity of the acquired data.

Conclusion

Surgeons should consider performance status rather than the sum of co-morbidities in future risk prediction. In this study, we identified potential parameters that can be preoperatively easily assessed and are feasible to collect in clinical routine. ECOG PS and BMI should be given more attention in clinical decision-making, treatment planning and patient counseling. A high intraoperative use of norepinephrine and FFP during cytoreductive surgery should lead to interdisciplinary communication between surgeons and anesthesiologists to give more awareness of the vulnerability of patients for complications.

References

1. Chang S-J, Hodeib M, Chang J, Bristow RE (2013) Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. Gynecol Oncol 130(3):493–498. https://doi.org/10.1016/j.ygyno.2013.05.040
2. Pomec C, Jeyarajah A, Oram D et al (2007) Cytoreductive surgery for ovarian cancer patients with a high
36. Schwarte LA, Schwartges I, Schober P, Scheeren TWL, Fournell A, Picker O (2010) Sevoflurane and propofol anaesthesia differentially modulate the effects of epinephrine and norepinephrine on microcirculatory gastric mucosal oxygenation. Br J Anaesth 105(4):421–428. https://doi.org/10.1093/bja/aeq215

37. Gelman S, Mushlin PS, Weiskopf RB (2004) Catecholamine-induced changes in the splanchnic circulation affecting systemic hemodynamics. Anesthesiology 100(2):434–439. https://doi.org/10.1097/00000542-200402000-00036

38. Bartl T, Schwameis R, Stift A et al (2018) Predictive and prognostic implication of bowel resections during primary cytoreductive surgery in advanced epithelial ovarian cancer. Int J Gynecol Cancer 28(9):1664. https://doi.org/10.1097/IGC.0000000000001369

39. Grimm C, Harter P, Alesina PF et al (2017) The impact of type and number of bowel resections on anastomotic leakage risk in advanced ovarian cancer surgery. Gynecol Oncol 146(3):498–503. https://doi.org/10.1016/j.ygyno.2017.06.007

40. Hunsicker O, Fotopoulou C, Pietzner K et al (2015) Hemodynamic consequences of malignant ascites in epithelial ovarian cancer surgery. Medicine (Baltimore). https://doi.org/10.1097/MD.000000000002108

41. Yang L, Stanworth S, Hopewell S, Doree C, Murphy M (2012) Is fresh-frozen plasma clinically effective? An update of a systematic review of randomized controlled trials. Transfusion 52(8):1673–1686. https://doi.org/10.1111/j.1537-2995.2011.03515.x (quiz 1673)

42. Shiba H, Ishida Y, Haruki K et al (2013) Negative impact of fresh-frozen plasma transfusion on prognosis after hepatic resection for liver metastases from colorectal cancer. Anticancer Res 33(6):2723–2728

43. Cata JP, Wang H, Gottumukkala V, Reuben J, Sessler DI (2013) Inflammatory response, immunosuppression, and cancer recurrence after perioperative blood transfusions. Br J Anaesth 110(5):690–701. https://doi.org/10.1093/bja/aet068

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.