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The impact of type and number of bowel resections on anastomotic leakage risk in advanced ovarian cancer surgery

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HIGHLIGHTS

- Anastomotic leakage (AL) rate after debulking surgery with bowel resection was 6.9%.
- Rectosigmoid resection seems to be associated with the highest rate of AL.
- Multiple bowel resections led to a slight but not significant increase in AL rate.
- We were not able to identify predictive factors for AL.

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ABSTRACT

Objective. To identify risk factors for anastomotic leakage (AL) in patients undergoing primary advanced ovarian cancer surgery and to evaluate the prognostic implication of AL on overall survival in these patients.

Methods. We analyzed our institutional database for primary EOC and included all consecutive patients treated by debulking surgery including any type of full circumferential bowel resection beyond appendectomy between 1999 and 2015. We performed logistic regression models to identify risk factors for AL and log-rank tests and Cox proportional hazards models to evaluate the association between AL and survival.

Results. AL occurred in 36/800 (4.5%; 95% confidence interval [3%–6%]) of all patients with advanced ovarian cancer and 36/518 (6.9% [5%–9%]) patients undergoing bowel resection during debulking surgery. One hundred fifty-six (30.1%) patients had multiple bowel resections. In these patients, AL rate per patient was only slightly higher (9.0% [5%–13%]) than in patients with rectosigmoid resection only (6.9% [4%–10%]), despite the higher number of anastomosis. No independent predictive factors for AL were identified. AL was independently associated with shortened overall survival (HR 1.9 [1.2–3.4], $p = 0.01$).

Conclusion. In the present study, no predictive pre- and/or intraoperative risk factors for AL were identified. AL rate was mainly influenced by rectosigmoid resection and only marginally increased by additional bowel resections.

1. Introduction

Surgical treatment is, next to platinum-based chemotherapy, the crucial treatment modality of advanced epithelial ovarian cancer (EOC) [1]. Postoperative residual disease is the most important prognostic parameter for patients with EOC and is accessible for therapeutic modification. The goal of debulking surgery is to achieve no macroscopic residual disease at the end of surgery [1–4]. In advanced EOC, it is frequently necessary to perform radical surgery including upper

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abdominal surgery and some type of bowel resection to achieve a complete resection without any macroscopic residual disease [4–6].

Anastomotic leakage (AL) is the most common severe complication after bowel resection. Many studies have investigated the feasibility of rectosigmoid resection (RSR) in the treatment of patients with advanced EOC [6–8]. RSR is frequently accompanied with some other type of bowel resection in advanced EOC. In a literature search, only one study reported AL rates in patients with multiple bowel resections comprising 42 patients with AL. Of note, this study included patients with primary and recurrent ovarian cancer resulting in a heterogeneous study cohort [9]. Thus, the information about the AL risk in patients with primary advanced EOC experiencing multiple bowel resections at the time of debulking surgery is limited. Furthermore, association between type of bowel anastomosis and AL rate, association between number of bowel anastomosis and AL rate as well as predictive risk factors for AL and, finally, the prognostic impact of AL in advanced EOC should be evaluated.

We aimed to describe AL rates (per patient and per anastomosis) in a large cohort of patients truly at risk – i.e., only patients with any type of full circumferential bowel resection beyond appendectomy - undergoing treatment in a certified and ESGO accredited high volume tertiary cancer center specialized on ovarian cancer. Additionally, we aimed to identify pre- and intraoperative risk factors for AL.

2. Patients and methods

Our institutional ovarian cancer database was analyzed. Between January 1999 and December 2015, 1132 consecutive patients with primary advanced EOC were treated by our team at the gynecologic oncology centers 1999–2010, Horst-Schmidt-Kliniken, Wiesbaden and since 2011 in the Kliniken-Essen-Mitte, Essen, both Germany. Only patients with primary advanced high-grade serous epithelial ovarian cancer (HGSOC) FIGO III–IV (n = 800) were included in the present study to provide a homogenous cohort of patients. We excluded all patients, who did not undergo full circumference bowel resection or received an appendectomy only (n = 282 [35.3%]). Thus, we included 518 (64.8%) patients with primary advanced HGSOC who experienced at least one bowel resection during primary or interval debulking surgery. Surgery was performed by accredited gynecological oncologists and all anastomoses were performed by an interdisciplinary surgical team including accredited visceral surgeons. With respect to bowel surgery, it was aimed to avoid a Hartmann stoma in all patients. Thus, a protective stoma was performed in patients with more than two bowel resections, low performance status, very long duration of surgery (>480 min), anastomosis < 8 cm from the anal verge, and/or inflammatory bowel disease on surgeon's discretion. Of note, due to the retrospective analysis there was no uniform algorithm over the whole study period for the performance of a protective stoma. Hartmann stoma without anastomosis was performed in selected patients with anastomosis < 5 cm from the anal verge, extensive intraabdominal inflammation and/or adhesions leading to a low chance for performance of an anastomosis in a subsequent surgery.

Preoperative bowel preparation including mechanical bowel preparation was performed until December 2010. From January 2011 patients received only one enema 2 h before surgery. Since January 2016 preoperative carbohydrate loading is performed routinely in all patients. All patients received intravenous antibiotic prophylaxis in the operating room before skin incision. Patients received a second dose if duration of surgery exceeded 240 min and/or in case of extensive blood loss (>1000 mL). Postoperatively, early food uptake and early mobilization on the first postoperative day was initiated.

AL was defined as follows: feculent fluid from drains, vaginal vault or wound; extravasation from anastomotic site verified by radiologic imaging with computer tomography and/or anastomotic leakage confirmed at revision surgery. All patients with suspicion for AL as above defined were operated on. Ileocecectomy with subsequent anastomosis of ileum and colon was included in the cohort of large bowel resections as anastomotic leakage rates are comparable to other large bowel resections [10–12]. In selected patients with only mildly elevated infection parameters and anastomotic leakage symptoms without signs for peritonitis and without persistent fever, anastomotic leakage was treated conservatively without surgery. Of note, due to our clinical algorithm CT- or ultrasound-guided drainage was not performed routinely in stable patients. Thus, only a minority of patients with anastomotic leakage had been treated conservatively without surgical intervention. As patients treated conservatively could not be identified comprehensively in our database and by additional chart review, they were excluded from the present analysis to minimize bias. All patients gave informed consent for documentation of clinical data in the associated clinical tumor registries and for clinical research and quality assurance analyses. Platinum-paclitaxel combination chemotherapy was recommended after surgery according to standard guidelines to all patients in the observation period [3,13,14].

2.1. Statistics

Standard statistical analyses were used to evaluate descriptive statistics such as mean, median, frequencies, and percentages: frequency (%) for categorical variables; median/range for skewed distributed metric variables; mean (standard deviation = SD) for normally distributed metric variables. AL rates were given with 95% confidence intervals to provide additional information about the rates observed in our study. The variables duration of surgery, blood loss, and surgical complexity score (SCS) are provided as binary variables using the median value as a cut-off. Chi square tests and Student's *t*-tests providing p-values and risk ratios (RR) (95% confidence interval [CI]) were used where appropriate to provide univariate analysis for risk factors for AL. A binary logistic regression model was performed to identify independent risk factors for AL. Uni- and multivariable survival analyses were performed using Kaplan-Meier and Cox proportional hazard models, respectively. A logistic regression model was conducted to analyze the association of AL and overall survival adjusting for potential confounding variables. Overall survival (OS) was calculated from the date of surgery to either the last follow-up or the date of death. All statistical tests were two-sided, and p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 20.0 (IBM Corporation, New York, USA).

3. Results

Initially, 800 patients with epithelial high-grade serous ovarian cancer FIGO III–IV undergoing debulking surgery were included in the present study. Of these, 518 (64.8%) patients had bowel resection as part of debulking surgery. This resulted in a complete resection rate of 63.7%. Overall, 36 patients experienced an anastomotic leakage (AL). This translated in an AL rate of 4.5% (3%–6%) for all FIGO III–IV patients and of 6.9% (5%–9%) for the 518 patients with bowel resection (Fig. 1). One hundred fifty-six of the 518 (30.1%) patients had multiple bowel resections resulting in 689 bowel anastomoses. This translated in an overall AL rate of 5.2% (4%–7%) per anastomosis. Patients with resection of the rectosigmoid (RSR) had slightly higher AL rates (n = 433; 7.6% [5%–10%] per patient) compared to patients with bowel resection other than RSR (n = 85; 3.5% [0%–7%] per patient), however, differences were not significant (p = 0.24). This was partially caused by the higher percentage of multiple resections in the group of patients with RSR. AL rates per anastomosis were also slightly higher in the group with RSR only or additional other bowel resections (RSR 5.6% [4%–7%] per anastomosis) compared to the group of patients with bowel resection other than RSR (3.1% [0%–7%] per anastomosis) pointing at the highest risk for RSR among all bowel resections. But again, the difference was not statistically significant (p = 0.46).

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