



Pattern of and reason for postoperative residual disease in patients with advanced ovarian cancer following upfront radical debulking surgery



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HIGHLIGHTS

- In 90% receiving upfront debulking surgery complete resection rate was 66.4%.
- 80% of patients with residual tumor had miliary carcinomatosis on intestinal serosa.
- 90% of patients benefit from upfront debulking surgery.

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ABSTRACT

Objective. Describing the pattern of and reasons for post-operative tumor residuals in patients with advanced epithelial ovarian cancer (AOC) operated in a specialized gynecologic cancer center following a strategy of maximum upfront debulking followed by systemic chemotherapy.

Methods. All consecutive AOC-patients treated between 2005 and 2015 due to stages FIGO IIIB/IV were included in this single-center analysis.

Results. 739 patients were included in this analysis. In 81 (11.0%) patients, chemotherapy had already started before referral. Of the remaining 658 patients, upfront debulking was indicated in 578 patients (87.8%), while 80 patients (12.8%) were classified ineligible for upfront debulking; mostly due to comorbidities. A complete tumor resection was achieved in 66.1% of the 578 patients with upfront surgery, 25.4% had residuals 1–10 mm and 8.5% had residuals exceeding 10 mm, and 12.5% of patients had multifocal residual disease. Most common localization was small bowel mesentery and serosa (79.8%), porta hepatis/hepatoduodenal ligament (10.1%), liver parenchyma (4.3%), pancreas (8.0%), gastric serosa (3.2%), and tumor surrounding/infiltrating the truncus coeliacus (2.7%); 14.9% of the patients had non-resectable supra diaphragmatic lesions. Size of residual tumor was significantly associated with progression-free and overall survival.

Conclusions. Upfront debulking for AOC followed by systemic chemotherapy was our main treatment strategy in almost 90% of all patients. The majority experienced a benefit by this approach; while 11.7% of patients probably did not. Understanding sites and reason for residual disease may help to develop adequate surgical training programs but also to identify patients that would better benefit from alternative treatment strategies.

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1. Introduction

Epithelial ovarian cancer is the second most common genital cancer in women and accounts for the majority of deaths from gynecologic malignancies in Western countries. Approximately 70% of women with newly diagnosed ovarian cancer will present at an

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advanced stage [1,2]. Quality of treatment is an independent prognostic parameter [3]. Maximal effort cytoreductive surgery represents a major therapeutic cornerstone. Primary goal of surgery is apart of obtaining tissue biopsies, to also conduct an adequate intra-abdominal staging in presumed early ovarian cancer and complete tumor resection in advanced forms of the disease. Improved surgical techniques have resulted in higher rates of total macroscopic tumor clearance. Several analyses have shown a significant correlation of survival with postoperative residual disease [4]. For example the overall survival of patients with International Federation of Gynecology and Obstetrics (FIGO) IIC ovarian cancer could be increased from 34.2 months after incomplete resection to 81.1 months after complete resection [5]. The incorporation of extended surgical techniques in the upper abdomen such as diaphragmatic peritoneal stripping or splenectomy has been shown to increase rates of complete tumor resection [6,7] and consequently progression-free and overall survival [8,9]. Furthermore, even though cytoreduction to a maximal tumor diameter of 1–10 mm may provide a less pronounced benefit compared to complete resection, it has clearly shown to have a positive prognostic impact compared to larger size of residual disease [5]. Therefore, debulking surgery has two distinct goals: complete tumor resection as the highest priority or if this is not possible at least tumor resection to smallest residual disease. Postoperative residual disease larger than 10 mm appears not to have any prognostic survival benefit [5] and therefore novel therapeutic strategies for this subgroup are warranted.

This exploratory analysis describes the pattern of and reasons for postoperative residual disease in patients with advanced ovarian cancer following upfront radical debulking surgery in a specialized gynecologic oncology surgical center.

2. Materials and methods

A prospectively operating clinical database was analyzed. Patients were treated in the Department of Gynecology and Gynecologic Oncology at the Dr. Horst Schmidt Klinik Wiesbaden between January 2005 and December 2010 or in the Department of Gynecology and Gynecologic Oncology at Kliniken Essen-Mitte between January 2011 and September 2015, by the same surgical team led by one of the authors (AdB). All consecutively treated patients with advanced invasive epithelial ovarian cancer FIGO IIIB–IVB (N = 739) were included in the analysis. The annual number of newly presenting patients increased steadily during the entire period from 71 in 2005/2006 to 162 in the last 24 months. In 161 patients (21.8%) maximal effort surgery was not indicated, or neoadjuvant chemotherapy had begun already elsewhere (Fig. 1). The latter accounted for 81 patients while we indicated upfront chemotherapy (mainly with the intent for interval debulking surgery) in another 80 patients (10.8% of all patients not having already started upfront chemotherapy outside). Surgery for diagnostic purposes only or no surgery at all was performed in 73 patients, the majority of them having a poor performance status. Sixty nine of those patients (94.5%) were treated primarily in our department and 4 patients (5.4%) were referred for further treatment from referring hospitals (Fig. 1). Significant cytoreduction and suboptimal debulking were defined as tumor residuals ranging between 1 and 10 mm and > 10 mm, respectively. All residuals were counted per person and we did not separate intraabdominal and extraabdominal disease. If pre-surgical staging revealed pleural effusion, cytologic examination was conducted, and the pleural cavity was examined during diaphragmatic surgery. If pre-surgical staging revealed non-resectable thoracic metastases, effort to remove tumor in the abdominal cavity was adapted and

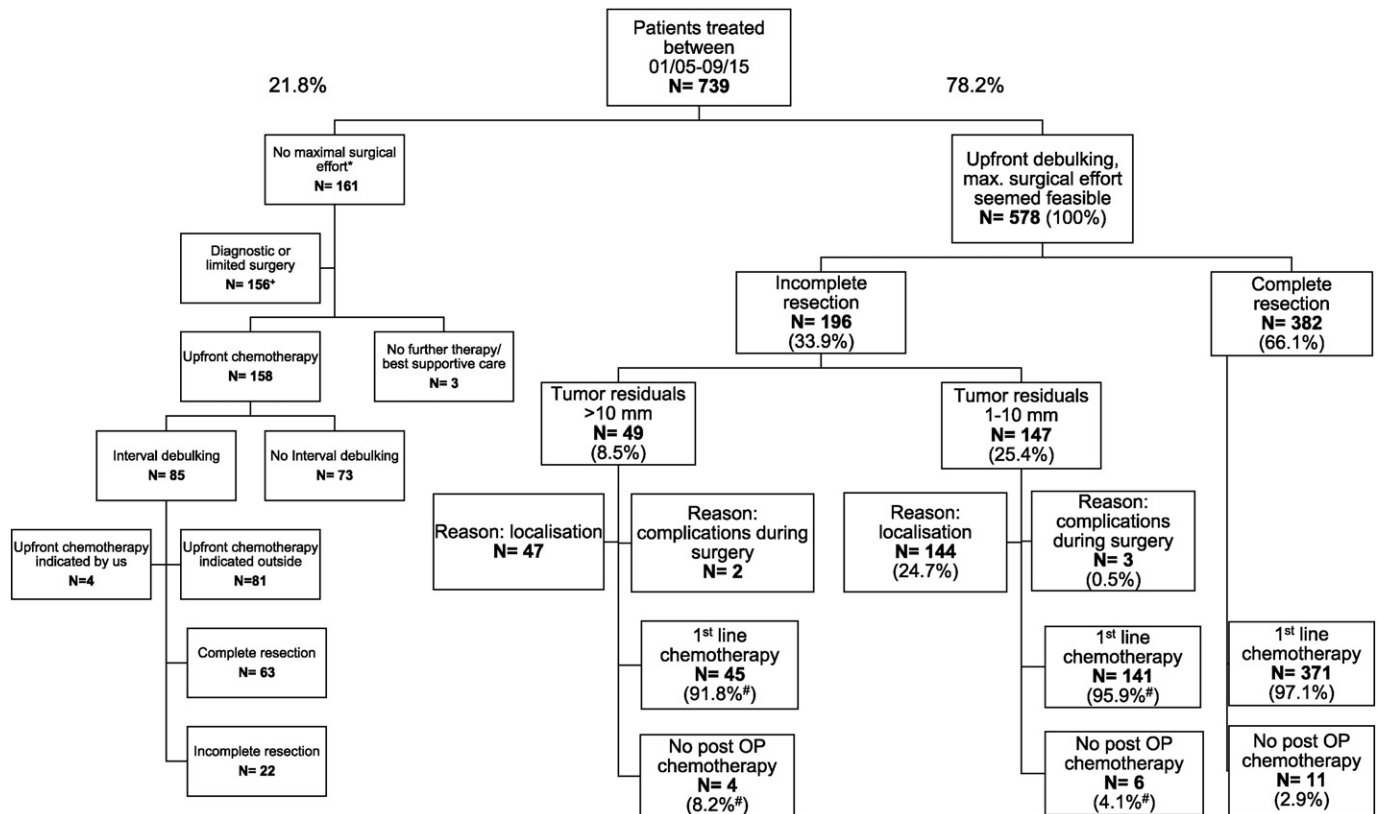


Fig. 1. All patients treated with invasive epithelial ovarian cancer FIGO IIIB–IV between 01/2005 and 09/2015; *not regarded as feasible for radical surgery (169/753 patients) due to comorbidity (4/169 patients) or started upfront chemotherapy already outside (83/165) or at our center (82/165), which reflects 10.9% of all patients treated in our center.

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