Re-operation outcome in patients referred to a gynecologic oncology center with presumed ovarian cancer FIGO I-IIIA after sub-standard initial surgery

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Abstract

Background: Surgery is the mainstay of treatment for early ovarian cancer both as therapeutic and comprehensive staging. Only the latter allows appropriate tailoring of systemic treatment. However, the compliance with guidelines for comprehensive staging has been reported to be only moderate and, therefore, re-staging procedures are commonly indicated to avoid undertreatment. The purpose of our study was to evaluate re-operation in a tertiary gynecologic oncology unit after primary operation for presumably ovarian cancer FIGO I-IIIA in general gynecology departments.

Material and methods: Forty consecutive patients after primary surgery in the outside institutions for presumed early ovarian cancer with assumed tumor spread limited to the pelvis (FIGO I-IIIA) admitted to our department between 1999 and 2007 were included. In 35 cases re-staging surgery in our unit was indicated. The intra- and post-operative results were compared with initial diagnosis and sites of undetected disease were evaluated. Reasons for re-staging and referral pattern were studied.

Results: 40 patients were enrolled of whom 53% came by self-referral. Only 18% were referred by the primary surgeon and the remaining patients were referred by their home gynecologist. Only 5 patients (13%) were classified as having had a comprehensive staging by surgical records and pathology reports and 35 patients underwent comprehensive re-staging laparotomy after which 20 patients (50%) experienced an upstaging including 13 patients with final diagnosis of FIGO stage IIIC. Most frequent sites of primarily undetected tumor were peritoneum (pelvic 34%, diaphragm 13%, paracolic 8%), lymph nodes (para aortic 32%, pelvic 11%), intestines 24%, and residual omental tissue 18%. The indication for post-operative chemotherapy was modified in 53% of patients.

Conclusion: Comprehensive staging of presumed early ovarian cancer has been described as major problem especially outside gynecologic oncology units. Re-staging results in our department confirmed this deficiency by showing a considerable proportion of upstaging associated with alterations of recommendations for systemic treatment. However, series like this may even underestimate the problem, because incomplete staging is unfortunately accompanied by non-systematic referral practices not reflecting staging quality.

Introduction

The pivotal study by Young RC et al. demonstrated in 1983 [1] the deficiency in comprehensive staging of presumed early ovarian cancer. Since then, sparse studies confirmed this initial observation showing a considerable lack regarding adherence to staging guidelines especially outside of specialized gynecologic oncology centers [2,3]. In particular, the authors noted up to 30% upstaging rate in patients who underwent primary surgery.

Analysis of pattern of care for early ovarian cancer have reported improved quality in more specialized departments resulting in guidelines recommendations for consultation or referral to a reference center to enhance patients’ outcome [4–7]. Comprehensive staging surgery for presumed early ovarian cancer has been described as important prognostic factor for the patients’ outcome [8–14]. It fulfills two pre-requisites for adequate therapy, namely complete removal of tumor tissue and identification of patients who need further adjuvant systemic therapy. The latter helps to avoid unnecessary treatment in those who do not need it and to apply adequate treatment to those who probably benefit.
The purpose of our study was to evaluate the impact of re-staging surgery for presumed ovarian cancer FIGO I-IIIA on both surgical outcome and planning of adjuvant chemotherapy. In addition, we identified pathways and referral practice of patients who finally attended a tertiary gynecologic oncology unit for this purpose.

Materials and methods

Four-hundred-ten consecutive patients with initial diagnosis of invasive epithelial ovarian cancer attended the department of Gynecology and Gynecological Oncology at the Dr. Horst Schmidt Klinik Wiesbaden between July 1999 and June 2007. This study did not include patients who attended for consultation or presented initially in our unit with recurrent disease, had non-epithelial ovarian neoplasm, or borderline tumors. All patient data are documented prospectively in a clinic tumor registry and patients are followed with at least annual actualization of the database. For this retrospective analysis we selected all consecutive patients who presented with presumed early ovarian cancer and tumor spread macroscopically limited to the pelvis (FIGO I-IIIA) as reported after initial surgery elsewhere. According to our in-house standard we reviewed patients’ charts, surgical and histology reports received from the outside institutions and qualified patients for the re-staging laparotomy at our department if we regarded staging procedures as not comprehensive. Patients with comprehensive staging surgery outside received only adjuvant therapy (or no systemic treatment) at our unit. In case surgery was planned, every patient underwent general physical and gynecological examination including abdominal and vaginal ultrasonography, chest X-ray if not performed within the last 6 months, CA-125 combined with standard blood tests, and mammography if not performed within the last 12 months. In cases when results of standard pre-operative staging methods were questionable further examinations for example computer tomography or magnetic resonance were indicated. The re-staging surgery were performed following our departments’ standards based on national guidelines [15] and consisted of midline incision, peritoneal washings, inspection and palpation of the abdominal cavity, peritoneal biopsies (pouch of Douglas, bladder, pelvic sidewalls, paracolic gutter, diaphragm), bilateral salpingooophrectomy, total abdominal hysterectomy, at least infracolic omentectomy, appendectomy in case of non-serous histologic type, and systematic para aortal and pelvic lymphadenectomy. A fertility sparing approach leaving the uterus and the none affected adnexe in situ was applied in young patients with histologic type, and systematic para aortal and pelvic lymphadenectomy was sparse. Only 2 of the 35 patients (6%) who were operated during initial surgery in 35 patients deemed for the time of initial surgery outside, however this criterion was not used for indication of re-operation if all other criterions of comprehensive surgery had been fulfilled (Table 1). In 12 cases patients obtained Pfannenstiel incision. Four patients had received even two surgical approaches not recommended by the national guidelines, namely laparoscopy followed by Pfannenstiel incision. Overall, laparoscopy was the only surgical approach in 9 patients in whom a lap-sac was used in only 2 patients. Total abdominal hysterectomy had been performed in 6 of the 35 patients (17%), only 13 patients (37%) had bilateral salpingoophorectomy, 19 patients (54%) had unilateral salpingoophorectomy, and omentectomy had been performed in only 4 patients (11%). Random peritoneal biopsies were taken in only 11 (31%) patients. The frequency of lymphadenectomy was sparse. Only 2 of the 35 patients (6%) who were scheduled for re-operation had received a pelvic and lower para aortic lymphadenectomy, and in one patient only pelvic lymph nodes were resected. One patient had received a rectum resection with subsequent end-to-end anastomosis initially (Table 1). A fertility sparing approach was performed in one patient with presumed FIGO stage IA G2.

Results

Overall, 40 patients presented with presumed ovarian cancer FIGO I-IIIA after initial surgery in an outside hospital. None of these patients had a comprehensive staging laparotomy according to our departments standards thus not qualifying for re-staging procedures. In contrast, 35 patients (87%) were deemed candidates for re-staging laparotomy. All patients agreed and were finally re-operated in our unit. The median patient age was 46 years (range 22–69). Time between primary surgery and re-staging laparotomy at our department ranged between 20 and 340 days (median 53 days). 68% of the initial laparotomies were performed in hospital based gynecological departments and 32% by office based gynecologists. The vast majority was not referred for re-operation (82%). In 53% the reason of admission to our department was patient’s self-referral and in 29% the home gynecologist performed the referral for further therapy (including some patients in whom the home gynecologist had some uncertainty if the performed surgery had been comprehensive). Only 18% of the patients were referred by the physician who performed the initial surgery either for consultation with respect to re-operation or for consultation regarding adjuvant chemotherapy.

Among five outside comprehensively operated patients one was diagnosed with stage IA, two with IC, one with IIA and one with IIB. Three of them presented poorly differentiated tumor G3, and two G2. Out of the 35 patients who underwent re-staging surgery eleven (31%) were initially diagnosed with stage FIGO IA; further ten (29%) with FIGO IC; five (14%) with FIGO IIA; four (11%) with FIGO IIB, two (6%) with FIGO IIC, and three (9%) with FIGO IIIA. About one third of patients had an undifferentiated tumor with Grading G3 (37%) and only 5 patients had well differentiated tumor histology G1 (14%).

Most of the 35 patients who were deemed for re-operation had an inadequate incision for the comprehensive staging procedures at the time of initial surgery outside, however this criterion was not used for indication of re-operation if all other criterions of comprehensive surgery had been fulfilled (Table 1). In 12 cases patients obtained Pfannenstiel incision. Four patients had received even two surgical approaches not recommended by the national guidelines, namely laparoscopy followed by Pfannenstiel incision. Overall, laparoscopy was the only surgical approach in 9 patients in whom a lap-sac was used in only 2 patients. Total abdominal hysterectomy had been performed in 6 of the 35 patients (17%), only 13 patients (37%) had bilateral salpingoophorectomy, 19 patients (54%) had unilateral salpingoophorectomy, and omentectomy had been performed in only 4 patients (11%). Random peritoneal biopsies were taken in only 11 (31%) patients. The frequency of lymphadenectomy was sparse. Only 2 of the 35 patients (6%) who were scheduled for re-operation had received a pelvic and lower para aortic lymphadenectomy, and in one patient only pelvic lymph nodes were resected. One patient had received a rectum resection with subsequent end-to-end anastomosis initially (Table 1). A fertility sparing approach was performed in one patient with presumed FIGO stage IA G2.

**Table 1**

Surgical procedures missing during initial surgery in 35 patients deemed for the re-operation in our unit.

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Careful review of initial surgical and pathology reports revealed 5 (13%) patients having had a comprehensive staging laparotomy according to our departments standards thus not qualifying for re-staging procedures. In contrast, 35 patients (87%) were deemed candidates for re-staging laparotomy. All patients agreed and were finally re-operated in our unit. The median patient age was 46 years (range 22–69). Time between primary surgery and re-staging laparotomy at our department ranged between 20 and 340 days (median 53 days). 68% of the initial laparotomies were performed in hospital based gynecological departments and 32% by office based gynecologists. The vast majority was not referred for re-operation (82%). In 53% the reason of admission to our department was patient’s self-referral and in 29% the home gynecologist performed the referral for further therapy (including some patients in whom the home gynecologist had some uncertainty if the performed surgery had been comprehensive). Only 18% of the patients were referred by the physician who performed the initial surgery either for consultation with respect to re-operation or for consultation regarding adjuvant chemotherapy.

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Six patients (15%) with FIGO stages IIA (1 pat.), IIB (1 pat.), IIC (2 pat.), and FIGO IIIA (2 pat.) had received adjuvant chemotherapy before admission to our department. All of these patients had received platln/taxane combinations (median 5.5 cycles, range 4–6 cycles).

The primary surgeons had reported complete tumor resection without residual disease in 29 patients (73%) and residual disease after primary surgery was reported in 11 patients (27%) of whom 9 were classified as inoperable by the primary surgeon.

Overall, 30 of the 35 re-operated patients (86%) received a complete resection without visible residual disease and all patients received a comprehensive staging. We did not detect any residual tumor during re-operation in 14 patients (40%). In contrast, we found residual tumor during re-operation at our unit in 21 patients (60%) including 5 of the 6 patients who had already started adjuvant chemotherapy outside our institution. The pelvic peritoneum (34%) and para aortic lymph nodes (32%) were the most frequent localization of residual tumor (Table 2). Of the 21 patients with residual tumor detected during re-operation complete resection could be achieved in 16 patients including the majority of the 9 patients regarded as inoperable. The 5 patients in whom we could not achieve a complete resection of all macroscopic tumor had initially presumed FIGO stages IA (1 pat.), IIB (1 pat.), IIC (1 pat.), IIIC (2 pat.), and IIIA (1 pat.). Reasons for incomplete surgery were not resectable lesions involving the root of mesentery, or the duodenum and/or pancreas. Three of these 5 patients ended up in subtotal debulking with residues with largest diameter of less then 1 cm.

The comprehensive re-staging laparotomy performed at our department resulted in upstaging of 20 of 35 patients (57%) in whom a re-operation had been indicated. The overall upstaging rate was 50% for the whole study cohort including the 5 patients whom we could not achieve a complete resection of all macroscopic tumor had initially presumed FIGO stages IA (1 pat.), IIB (1 pat.), IIIC (2 pat.), and IIIA (1 pat.). The type of incision at the initial surgery did not significantly predict upstaging. Upstaging was observed in all presumed initial stages of disease. In detail, we observed upstaging in presumed FIGO stage IA in 5 patients (42% of all presumed FIGO IA tumors); in 4 patients with presumed FIGO IC (33%), in 4 patients with presumed FIGO IIA (67%), in 3 patients with presumed FIGO IIB (60%), in 1 patient with presumed FIGO IIC (50%), and in all 3 patients with presumed FIGO IIIA (100%). Although upstaging occurred in all histological grades, we observed increasing rates according to differentiation grade: G1 – upstaging in 1 of 5 patients (20%), G2 – 9 of 18 patients (50%), and G3 – 10 of 16 patients (63%). Specific histological sub-types were not associated with different rates of upstaging, however subgroups were small. An upstaging was documented in 15 of 25 patients (60%) with serous ovarian cancer, in 3 of 4 patients (75%) with undifferentiated cancer, and in 3 of 6 patients (50%) with endometroid histology. Mucinous, clear cell and mixed histopathological types were diagnosed together in only 5 patients in our cohort.

A modification of the indication for chemotherapy was observed in 21 (60%) patients after comprehensive re-staging. All these patients fulfilled the criteria for receiving combination chemotherapy instead of single agent monotherapy. Furthermore, this subgroup included 6 of the 9 (67%) patients in whom the initially treating institution had not indicated any systemic treatment.

The median blood loss was 600 mL (range 50–2000) and 14 patients (40%) received blood products (fresh frozen plasma or transfusions). Major complications occurred in three patients (9%). The first patient developed a leakage after small intestine surgery which required surgical revision and drainage. Additionally, this patient developed a deep vein thrombosis which was conservatively treated. Finally, this patient recovered completely. The second patient suffered from ureter injury of the ureter with immediate surgical repair and had bladder dysfunction which relieved after conservative treatment for few weeks. The third patient died 38 days after re-staging surgery due to cardiac arrest. This patient had already pre-existing cardiac dysfunction which was probably underestimated pre-operatively. The most common minor complication was urinary tract infection which occurred in 9 patients (26%) and resolved after antibiotic therapy. All post-operative complications are listed in Table 4.

### Discussion

The present study confirms data published already 25 years ago and indicates lack of improvement regarding staging surgery for presumed early ovarian cancer outside specialized gynecologic oncology institutions. The upstaging rate observed in our series as well as the associated complication rate is comparable to data...
reported by others in preceding decades [1–3,17,18]. Para aortic lymph nodes were the second most frequent localization of residual disease causing upstaging in the present series. Others have reported positive para aortic lymph nodes during upstaging surgery in only 7–12% compared to 32% in our cohort [12,18,19]. The slightly higher rates of upstaging in our cohort compared to data from others may be based on different surgical techniques. All our patients received systematic pelvic and para aortic lymphadenectomy. One third of positive para aortic lymph nodes was already microscopic metastases which might not be detected by palpation guided lymph node resection or limited sampling techniques [14,20–22]. However, the prognostic value of microscopic lymph node metastasis is not completely clear and balancing the higher surgical burden of systematic lymphadenectomy against slightly higher detection rates remains an area of further research.

This study raises the question why gynecologists continuously perform suboptimal management of early ovarian cancer observed in each study evaluating this issue [4,23]. McGowan et al [24] reported already more than 20 years ago that initial staging laporan-tomographies for ovarian cancer performed by gynecologist/obstetrician compared to general surgeon were complete in only 52% and 35%, respectively. In contrast 97% of staging procedures performed by gynecologists’ oncologist were regarded as comprehensive. Many studies from different countries confirmed superior completeness of staging when performed by gynecologists’ oncologists and reported even lower rates of comprehensive staging outside specialized departments [4,5,12,25,26]. The initial staging operations in our study cohort were performed by hospital based gynecologists in 68% but none of the operations had been performed by gynecologic oncologists which might explain the disappointing results. The lack of comprehensive staging reflects not only a theoretical problem but implies a serious risk of exposing harm and risk to the patients. The latter is obvious if considering that re-staging could detect visible tumor in two thirds of patients who were told that they were free of any residuals after initial surgery what in case of no re-operation and no complete cytoreduction followed by standard chemotherapy might not achieve the optimal benefit for the patient [4,15]. Furthermore, indication for systemic treatment based on insufficient surgical data had to be changed in a considerable proportion of patients. Both medical overtreatment and undertreatment may result from incomplete staging. Overtreatment might expose the patient unnecessarily to toxicity impairing quality of life and undertreatment may even reduce survival expectations. Results of recurrent ovarian cancer initially diagnosed in FIGO stage I after no adjuvant therapy showed that prognosis was deteriorated and similar to advanced ovarian cancer thus excluding a “concept of a second chance” [27].

The magnitude of this problem might be underrated in this retrospective and single center study. In our series, only 18% of patients were referred for further treatment by the institution that has performed the initial surgery being most probably a result of false classification of majority primary operations as complete debulking. Incomplete staging and consecutive insufficient planning of adjuvant therapy was commonly not associated with a systematic referral practice. The majority of included patients attended our unit by self-admission. The latter probably implies that an even higher rate of patients with deficient initial treatment will never attend a specialized unit. The prolonged time lap between incomplete initial surgery and re-operation may result in new tumor lesions leading to possible inoperability. This observation proves a considerable deficiency regarding cooperation between the less experienced units and specialized departments. Gersherson discussed this issue already in 2001 [28]. He suggested several potential explanations among them unregulated health care system, failure in education, inadequate communication skills, economical competition, and conflict of interests between specialists and disciplines. These reasons might also apply to the situation in Germany and both national and international scientific societies should focus on improvement in that particular area.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Authorship

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Study design: J. P. Grabowski, P. Harter, A. du Bois.

Definition of intellectual content: J. P. Grabowski, P. Harter, A. du Bois, C. Buhrmann, R. Hils.

Literature research: J. P. Grabowski, P. Harter, A. du Bois, S. Kommos.


Experimental studies: —

Data acquisition: J. P. Grabowski, P. Harter, A. Traut, S. Kommos.

Data analysis: J. P. Grabowski, P. Harter, A. Traut, S. Kommos.

Statistical analysis: J. P. Grabowski, A. Traut.


Manuscript editing: J. P. Grabowski, P. Harter, A. du Bois.

Manuscript review: J. P. Grabowski, P. Harter, A. du Bois.

References


