Gynecologic Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Outcome of patients with advanced ovarian cancer who do not undergo debulking surgery: A single institution retrospective review

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HIGHLIGHTS

- Debulking surgery is not feasible for up to 20% of patients.
- Chemotherapy alone can allow reasonable disease control in women unsuitable for IDS.
- Carboplatin plus paclitaxel should be used when possible.

ARTICLE INFO

Article history:
Received 24 July 2016
Received in revised form 30 October 2016
Accepted 1 November 2016
Available online xxxx

Keywords:
Advanced ovarian cancer
Surgery
Chemotherapy
Neoadjuvant
Debulking
Carboplatin
Paclitaxel

ABSTRACT

Objective. To assess the outcome of patients with advanced ovarian cancer (OC) who were treated without surgery, having received upfront chemotherapy and no interval debulking surgery (IDS).

Methods. Retrospective analysis of medical and chemotherapy records of consecutive patients with OC between 2005 and 2013 at UCL Hospitals London, UK who received neoadjuvant chemotherapy (NACT) was then found to be unsuitable for IDS following review by the multidisciplinary team.

Results. Eighty-three patients (18%) out of 467 receiving NACT did not undergo IDS. Median age was 70 years (range 33–88); out of these 83 patients, 43 (51.8%) presented with stage IV disease. Forty-three of these 83 patients received carboplatin and paclitaxel (CP) (51.8%) and 37 received carboplatin alone (C) (44.6%); 3 patients (3.6%) received other platinum-based combinations. Reasons for not proceeding to surgery were: poor response to chemotherapy after 3–4 cycles of NACT (61/83, 73.5%); comorbidities (12/83, 14.5%); patient decision (4/83, 4.8%). Six patients (7.2%) received <3 cycles of NACT due to a worsening clinical condition. The median overall survival (OS) for patients not undergoing IDS was 18 months (95% CI 10–20 months). Forty-four of 83 patients (53%) received >2 lines of chemotherapy. In a univariate analysis CP, age <70 years, and absence of comorbidities were factors influencing OS. In a multivariate analysis only having received CP remained independently associated with OS (HR 0.49, 95% CI 0.29–0.84).

Conclusions. Chemotherapy alone can provide reasonable disease control in patients unsuitable for IDS and CP should be used if possible.

1. Introduction

Epithelial Ovarian Carcinoma (EOC) is the leading cause of death from gynecological cancer in the Western World. For women presenting with advanced disease the 5-year survival rate is approximately 30% [1]. Survival of women with epithelial ovarian cancer has improved partly as a consequence of more aggressive surgery to achieve optimal cytoreduction, the use of platinum-based treatment and better treatment of recurrent disease [2]. Nonetheless, approximately 80% of patients who present with advanced disease develop progression or relapse and die within 5 years from diagnosis [3].

Optimal primary debulking surgery followed by platinum-based chemotherapy [3] is the recommended treatment for advanced ovarian cancer (FIGO III–IV). Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) can be considered an alternative first-line treatment for patients in whom primary cytoreductive surgery is

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http://dx.doi.org/10.1016/j.ygyno.2016.11.001
0090-8258/

not possible or contraindicated due to co-morbidity [4–6]. Recent studies have shown similar outcome to primary surgery when interval debulking surgery (IDS) is performed after three cycles of neoadjuvant chemotherapy followed by three post-IDS cycles of chemotherapy [4–6].

It has been estimated that in 10–25% [6–8] of patients surgical debulking may be not feasible even after NACT, due to poor response to chemotherapy, poor or worsening of performance status, significant co-morbidities, or patients desire to avoid extensive surgery that might require bowel resection.

For these women chemotherapy is the primary treatment. It is usually given with palliative intent but little is known about the outcome of these patients.

The aim of this retrospective study was to understand the natural history of patients with advanced stages of EOC, treated with chemotherapy alone.

2. Materials and methods

All women with a diagnosis of invasive EOC who were treated between January 2005 and December 2013 at UCL Hospitals, London UK were included in this audit. Data were collected between October and November 2014 by reviewing the medical records, radiological imaging, chemotherapy prescriptions and outcome information.

The inclusion criteria were as follows: (1) histologically confirmed diagnosis of epithelial ovarian cancer; (2) not suitable for primary or interval debulking surgery; (3) having received primary chemotherapy and (4) availability of medical records.

Staging was performed by Computed Tomography (CT) imaging and defined in accordance with the FIGO (International Federation of Gynecology and Obstetrics) classification for ovarian cancer. All patients are reviewed at the treatment by a multi-disciplinary team (surgeon, radiologist, oncologist and pathologist) regarding suitability for surgery or primary chemotherapy. The patients in this series represent those in whom NACT was agreed, and we report those who did not proceed to surgery after NACT. All patients had previously undergone histological review by a specialist in gynecological pathology. Patients with a borderline tumor or a non-epithelial tumor were excluded.

All patients were treated with platinum-based chemotherapy and underwent CT evaluation after 3 or 4 cycles of chemotherapy. They were assessed for surgery by the same Multidisciplinary Team. The key evidence related to the radiologic criteria for a poor overall improvement and consequently unsuitability for surgery were defined as follows: diffuse deep infiltration of the root of the small bowel mesentery, widespread bowel serosal involvement, multiple parenchymatous liver metastases, infiltration of the duodenum and/or pancreas and/or the large vessels of the hepatic-duodenal ligament, celiac trunk or behind the porta hepatis, multiple lung metastases, as has previously been described by others [9].

The medical charts were reviewed to obtain information on the reason for not undergoing surgery, the type of first line chemotherapy, dates of treatment and the reasons for dose reductions and delays. Whilst clear significant co-morbidity data were recorded, there was no systematic documentation of performance score. The Charlson Co-morbidity index (CCI) score [10] was used retrospectively to assess co-morbidity.

Response was assessed by physical examination, serial measurement of CA125, and computed tomographic imaging. Response at the end of treatment was assessed by CA125 according to GCIG criteria [11] and CT evaluation. Progression was defined by clinical or radiological findings and the time to progression was taken as the date of radiological evidence of progression. Further treatments were recorded and overall survival was calculated from the date of primary diagnosis to date of death or to last follow-up visit for the patients still alive. Median follow-up period was measured from the date of primary diagnosis to the time of last follow-up visit.

Chi-square or Fisher's exact test was used for comparison of categorical variables. A logistic regression model was applied to determine the effect of independent variables (age, grading, presence of comorbidities (CCI)/pulmonary embolism, stage, and histology) on the choice of chemotherapy. Survival was calculated using the Kaplan–Meier method. Log-rank test was used to compare survival between groups. Multivariate analysis for prognostic factors was performed by Cox's proportional hazards regression model. All p values were two-sided, and the p-value was set at 0.05. All statistical calculations were carried out using SPSS for Mac version 22.0 (SPSS Inc., USA).

3. Results

During the study period primary chemotherapy (NACT) was given to 467 patients with ovarian cancer and 83 patients (18%) did not proceed to surgery, and are the subject of this study.

The median age was 70 years (range 33–88 years). This age was taken to define two categories: greater or less that 70 years: the median age was 61 years (range 33–70) in the former, and 79 years (range 71–88) in the latter. Clinical and pathological characteristics of patients are described in Table 1. Ten patients (12%) had previous history of other cancers. Patients in the older group were more frequently affected by

Table 1
Patients' pathological and clinical characteristics.

	Total 83	<70 yrs 42 (50.6%)	>70 yrs 41 (49.4%)	P*
AGE (median)	70 (range 33–88)	61	79	
Comorbidities				0.15
Absence of comorbidities	37 (44.6%)	23 (54.8%)	14 (34.1%)	
CCI 1	25 (30.1%)	9 (21.4%)	16 (39%)	
CCI 2	17 (20.5%)	9 (21.4%)	8 (19.6%)	
CCI 3	4 (4.8%)	1 (2.4%)	3 (7.3%)	
PE				0.58
Yes	16 (19.3%)	8 (19%)	8 (19.5%)	
No	67 (80.7%)	34 (81%)	33 (80.5%)	
FIGO stage				0.39
IIIB	1 (1.2%)	1 (2.4%)	0	
IIIC	39 (47%)	17 (40.5%)	22 (53.7%)	
IV	43 (51.8%)	24 (57.1%)	19 (46.3%)	
Grade				0.51
G2	6 (7.2%)	4 (9.5%)	2 (4.9%)	
G3	71 (85.6%)	36 (85.7%)	35 (85.4%)	
Missing	6 (7.2%)	2 (4.8%)	4 (9.8%)	
Histology				0.61
Serous	75 (90.4%)	39 (92.8%)	36 (87.8%)	
Clear cell	1 (1.2%)	1 (2.4%)	0	
Mucinous	3 (3.6%)	1 (2.4%)	2 (4.9%)	
Endometrioid	1 (1.2%)	0	1 (2.4%)	
Unspecified adenocarcinoma	3 (3.6%)	1 (2.4%)	2 (4.9%)	
Reasons for not performing surgery				0.16
Deteriorating before 3 cycles	6 (7.2%)	4 (9.5%)	2 (4.9%)	
Comorbidities	12 (14.5%)	5 (11.9%)	7 (17.1%)	
Patient's choice	4 (4.8%)	4 (9.5%)	0	
Insufficient improvement with NACT	61 (73.5%)	29 (69%)	32 (78%)	
Chemotherapy				0.015
C	37 (44.6%)	12 (28%)	25 (61%)	
CP	43 (51.8%)	27 (64.2%)	16 (39%)	
Others platinum combinations	3 (3.6%)	3 (7.1%)		

PE: pulmonary embolism; CCI: Charlson comorbidity score; CT: chemotherapy; NACT: neoadjuvant chemotherapy; CP: carboplatin plus paclitaxel; C: carboplatin; IDS: interval debulking surgery; * Chi square test.

Please cite this article as: C. Marchetti, et al., Outcome of patients with advanced ovarian cancer who do not undergo debulking surgery: A single institution retrospective review, Gynecol Oncol (2016), http://dx.doi.org/10.1016/j.ygyno.2016.11.001