

## DEMOGRAPHIC PROFILE AND OUTCOMES OF ADVANCED EPITHELIAL OVARIAN CANCER

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### Abstract

**Background:** To study the epidemiological features and outcome of epithelial ovarian cancer patients treated at a tertiary care hospital.

**Methods:** We conducted a retrospective study at our institute to identify patients diagnosed with epithelial Ovarian Carcinoma (EOC) from 2013 to 2018. We studied the epidemiological profile and the outcome of the treatment in terms of response rates, Disease-free survival, and overall survival rates.

**Results:** A total of 238 patients were diagnosed with EOC over a period of 7 years. Out of 238 patients, complete pretreatment data was available for 197 patients. The median age at diagnosis was 59 years (range: 34–85 years). Totally 39 patients (16.38%) were younger than 45 years of age. The common presenting features were abdominal distension (82%), dysuria (43%), abdominal pain (40%), loss of appetite (36%), constipation (32%), shortness of breath (15%). serum CA125 levels were elevated in 73% cases at presentation

**Conclusion:** In conclusion, it is of extreme importance to identify the prognostic factors in patients with ovarian cancer to enable us to choose the most appropriate treatment strategy and to identify the risk of progression and death at follow-up. In our study, the patient age and FIGO clinical stage were the only independent prognostic factors reported.

**Keywords:** FIGO, Ovarian, Germ cell

### Introduction

Ninety percent of ovarian cancers are derived from coelomic epithelium. Germ cell tumors account for 5% of ovarian cancers and sex cord-stromal tumors approximately 7%.<sup>1</sup> The common epithelial ovarian cancers (EOCs) include high-grade serous (70%), endometrioid (10%), clear cell (10%), mucinous (3%), and low-grade serous carcinomas (<5%).<sup>2</sup> They all have different epidemiology, molecular profiles, clinical presentations, patterns of spread, response to chemotherapy, and hence different prognosis. About 70% of patients with EOC present with advanced disease, as a result of the lack of any satisfactory screening test and specific symptoms.

Complete resection during cytoreductive surgery is the most important independent prognostic factor in advanced EOC. Survival is inversely related to the residual disease after surgery. In a meta-analysis of 6885 patients with Stage III or IV ovarian carcinoma, Bristow *et al.*<sup>3</sup> found that each 10% increase in maximal cytoreduction rates was associated with a 5.5% increase in median survival time. A review of 11,999 patients with advanced ovarian cancer reported that the median overall survival (OS) for patients with no residual disease was 70 months, compared to 53 months for patients with 1–5 mm, 40 months for patients with 1–10 mm, and 30 months for patients with >10 mm ( $P < 0.001$ ).<sup>4</sup> The authors concluded that although the aim of cytoreductive surgery should be leaving no gross residual disease, there is still a significant benefit in trying to

achieve “optimal” residual disease status (i.e., <1 cm), because such patients have a 10 months longer median OS, compared to patients with suboptimal residual disease.

However, patients with advanced ovarian cancer who do not achieve optimal debulking at the end of primary cytoreductive surgery do not benefit from this procedure and are likely to experience morbidity associated with extensive surgery. Neoadjuvant chemotherapy (NACT) before cytoreductive surgery has been extensively studied in patients who are unlikely to attain optimal cytoreduction or are poor surgical candidates. Two randomized controlled trials, conducted by the European Organisation for Research and Treatment of Cancer (EORTC) and the Medical Research Council (MRC) Clinical Trials Unit, have shown no significant differences in progression-free (PFS) and OS between the group with primary cytoreduction and the one with NACT followed by interval cytoreduction.<sup>5</sup> The median PFS was 12 months for both the groups in the EORTC trial and the OS was 29 months and 30 months, respectively. Optimal cytoreduction, defined as largest residual tumor <1 cm, was achieved in 41.6% of patients after primary cytoreduction and 80.6% of the patient after interval cytoreduction. Postoperative death (within 28 days of surgery) and surgical morbidity were lesser in the interval cytoreduction surgery group.<sup>6</sup>

## Material and methods

This was a retrospective analysis. All patients had serum CA-125 levels and a contrast-enhanced CT scan of the abdomen and pelvis before treatment. The diagnosis of ovarian cancer was made on the basis of cytopathological evaluation of ascitic or pleural fluid or histopathological confirmation of biopsies from representative lesions, where necessary.

All new cases with advanced EOC were jointly assessed by the gynecologic and medical oncologists. Patients who had a good performance status and/or were likely to be optimally cytoreduced underwent primary cytoreduction followed by six cycles of adjuvant platinum-based chemotherapy (Paclitaxel and Carboplatin). Patients who were in poor general condition and/or not likely to be debulked optimally were offered NACT (Paclitaxel and Carboplatin) followed by interval cytoreduction and then adjuvant chemotherapy. Optimal cytoreduction was defined as no evidence of macroscopically visible residual disease or residual disease  $\leq 1$  cm. After the completion of primary treatment, patients were followed up 3–4 monthly for the first 2 years and 6 monthly thereafter. At each follow-up visit, a complete physical examination and serum CA-125 level was done. Imaging was advised in case patient presented with symptoms, or a rise in serum CA-125 levels (serological relapse).

Demographic data including age and education were obtained from the medical records. Clinical data included the extent and type of surgery, intra- and post-operative complications, and neoadjuvant and adjuvant chemotherapy protocols. The records were reviewed for follow-up details including recurrence, if any, date of recurrence and treatment of recurrent disease. PFS was calculated in months from the date of completion of treatment to the date of first recurrence or progression or death, whichever occurred earlier. OS was calculated in months from the date of completion of treatment to the date of death, either due to disease or any other cause.

Data analysis- Data was recorded as per Performa. The data analysis was computer based; SPSS-22 was used for analysis. For categorical variables chi-square test was used. For continuous variables independent samples's *t*-test was used. *p*-value  $<0.05$  was considered as significant.

## Results:

A total of 238 patients were diagnosed with EOC over a period of 7 years. Out of 238 patients, complete pretreatment data was available for 197 patients. The median age at diagnosis was 59 years (range: 34–85 years). Totally 39 patients (16.38%) were younger than 45 years of age. The common presenting features were abdominal distension (82%), dysuria (43%), abdominal pain (40%), loss of appetite (36%), constipation (32%), shortness of breath (15%). serum CA125 levels were elevated in 73% cases at presentation.

The most common histology was papillary serous cystadenocarcinoma (71%), followed by mucinous cystadenocarcinoma (18%), endometrioid carcinoma (3%) and clear cell carcinoma (8%). the surgical staging based on FIGO classification (Year) was stage I (4%), stage II (9%), stage III (69%), and stage IV (18%). the most common chemotherapy regimen used was paclitaxel-carboplatin duet (93%), either in neoadjuvant or adjuvant setting.

On analysis of survivals using the Kaplan-Meier estimates and log-rank statistics, it was found that age was not associated with PFS and OS, whereas both surgical debulking status and FIGO stage of the tumor were associated with survival outcomes.

## Discussion:

Various studies outside SSA have focused on the identification of prognostic parameters for EOC, and several parameters that have been suggested to be predictive of survival in ovarian cancer include age,<sup>19</sup> FIGO stage, postoperative residual tumor,<sup>7-9</sup> tumor histology,<sup>10</sup> histological grade,<sup>11</sup> presence of ascites,<sup>12</sup> and pretreatment serum concentrations of CA-125.<sup>13</sup> An analysis of four prospective phase III intergroup trials in Germany that was conducted in 2016 found that patients less than age 40 years had a better PFS and OS compared with those older than 40 years. This is similar to the studies by Winter et al in 2007<sup>14</sup> and Chang et al in 2015<sup>15</sup> but in sharp contrast to the report from the study by Gil-Ibañez et al<sup>16</sup> where age was not found to be a predictor of survival in patients with ovarian cancer. Our current study showed a significant predictive effect of age on progression-free survival but not OS. This may be because age has an impact on patient ability to cope with stress related to a chronic disease state, and the altered physiology of the elderly alters the pharmacokinetics and pharmacodynamics of upfront chemotherapeutic agents used in the treatment of ovarian cancer. According to the Gynecologic Oncology Group, an optimal surgical debulking is defined as when the residual disease is  $\leq 1$  cm. Previous studies have shown that the ability to achieve optimal surgical debulking is the most important predictor of ovarian cancer survival,<sup>9-11</sup> but this was not corroborated by our study. This may be due to the significant proportion of patients in this cohort (73.5%) who presented with advanced disease and because of the decreased likelihood of downgrading extensive disease by radical surgery and the poorer survival outcome of patients with high peritoneal cancer index, even after undergoing complete cytoreduction. We also reported that advanced FIGO stage of EOC independently predicted a reduced PFS similar to the finding by Yan et al<sup>17</sup> and Liu et al<sup>18</sup> but at variance with the report by GillIbañez et al.<sup>16</sup>

## Conclusion:

In conclusion, it is of extreme importance to identify the prognostic factors in patients with ovarian cancer to enable us to choose the most appropriate treatment strategy and to

identify the risk of progression and death at follow-up. In our study, the patient age and FIGO clinical stage were the only independent prognostic factors reported.

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