



Oncological and Reproductive Outcome in Epithelial Ovarian Cancer in Women Less than 30 Years of Age

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Abstract

Objective: The objective of this study is to evaluate oncological and reproductive outcome of epithelial ovarian cancers and its clinicopathological patterns in patients less than 30 years of age.

Methods: This is a retrospective, single center study and all the patients diagnosed with EOCs from 2014 to 2019 AD who underwent either primary surgery or completion surgery in this center were included in the study. Thirty-six patients with EOCs were identified and their clinicopathological characteristics, overall survival, progression free survival and reproductive outcomes were determined. Mean was used to describe continuous variables whereas frequency and percentages were used to describe categorical variables.

Results: The number of Epithelial Ovarian Cancers in women less than 30 years was 36 (8.07%). The mean age of the patients was 24. The most common mode of presentation was abdominal pain in cases followed by abdominal distension. The most common tumor subtypes were mucinous carcinoma followed by eight cases each of borderline serous and serous carcinoma. Most of the patients presented in early stage of disease. Twenty-two patients (61.12%) underwent fertility sparing surgery. Five patients had recurrence and there was one mortality. The median follow up period was 44 (14 - 90) months. Progression free survival was 37.41 months and overall survival was 44 months. The overall survival rate was 94.45%.

Conclusion: EOCs are rare in young patient and diagnosed at early stage. They have excellent prognosis with fertility sparing surgery and adjuvant chemotherapy and successful pregnancy can be achieved in most of the cases.

Keywords: Age Less Than Thirty Years; Malignant Epithelial Ovarian Cancer; Reproductive Outcome; Survival Outcome; Recurrence

Introduction

Epithelial Ovarian Cancer (EOC) is often found in postmenopausal women with only 10 to 15% found in premenopausal wom-

en [1]. The peak incidence of EOCs is at 60 to 65 years of age with less than 1% being found in women below 30 years [2]. In India, ovarian cancer is the third most common cancer among women [1]

and there is no exact data regarding the incidence of EOCs in young women less than 30 years of age. In young age group ovarian germ cell tumors constitute 70% of ovarian tumors [3].

The primary treatment for EOC is total hysterectomy plus bilateral salpingo-oophorectomy with complete surgical staging. Careful surgical staging is important for early EOC patients because around 30% of patients who undergo complete staging surgery are upstaged. Both open and minimal invasive surgery (MIS) can be used for staging and surgical treatment.

For young patient with a desire to preserve fertility, fertility sparing surgery (FSS) is safe for stages IA and IC grades 1 and 2 disease and stage IC1 according to the new FIGO staging system. According to NCCN guidelines Fertility sparing surgery (FSS) consist of unilateral salpingo-oophorectomy (USO) and comprehensive surgical staging. The ideal candidates are unilateral stage I tumors and/or low-risk ovarian tumors (i.e. early-stage, grade 1 tumors; borderline tumors) and Stage IB: BSO (preserving the uterus) and comprehensive surgical staging [4]. European Society for Medical Oncology (ESMO) recommends FSS for all stage IA and IC1 low-grade ovarian carcinomas [5].

Most of the previous studies have mentioned either of malignant ovarian germ cell tumors or combine both epithelial and non-epithelial ovarian cancers in young age groups. Epithelial and non-epithelia malignant ovarian tumors need to be studied separately as the natural history and treatment modalities are different.

Material and Methods

This is an ecological study conducted at VPS Lakeshore Hospital, Kerala, India. All the patients diagnosed with EOCs from 2014 to 2019 AD who underwent either primary surgery or completion surgery in this center were included in the study. Data were collected retrospectively from electronic medical records regarding demographic, clinical, surgicopathological characteristics, treatment patterns, recurrence, survival rates and reproductive outcome. Staging and histological classification was done according to The International Federation of Gynaecology and Obstetrics (FIGO) staging system and WHO classification respectively.

Depending upon the radiological findings, surgical stage and pathological results, patient either got a) an upfront surgery fol-

lowed by adjuvant chemotherapy or active surveillance or b) neo-adjuvant chemotherapy (NACT) followed by interval cytoreduction. Before commencing NACT pathological diagnosis was done by biopsy taken from the primary site or metastatic site. After completion of treatment, active surveillance with clinical examination, tumor markers and ultrasound was done. when clinically indicated or when recurrence was suspected additional radiological investigation like CT scan was taken.

Complete surgical staging means peritoneal washings, systemic examination of intra-abdominal viscera, peritoneal biopsies, omentectomy (total or infracolic), and bilateral pelvic and paraaortic lymphadenectomy whenever indicated. Fertility sparing surgery (FSS) refers to complete surgical staging and preservation of the uterus and at least part of one ovary.

Progression free survival (PFS) refers to the time between completion of treatment and the date of the first recurrence and overall survival (OS) refers to the time from diagnosis to date of death or last follow up which ever occurred first.

Data collection and entry were done in Microsoft Excel spreadsheet which was then imported to Statistical Package for Social Sciences (SPSS™) software version 20 for analysis. Continuous variables were presented in means and categorical variables were expressed as frequency and percentages.

Results

The total of ovarian malignancy was 509 during the study period, out of which 446 were EOCs. EOCs in women less than 30 years were 36 (8.07% among all the EOCs). Table 1 presents the clinicopathological features of the study population. The mean age \pm SD of presentation of the patient was 24.36 ± 4.4 years. Majority of them were in the third decade of life; 15(3.36%) of them were in the age group of 20-25 years and 16 (4.45%) in the age group of 25 - 30 years of age.

Total number of recurrence was five. Among 22 cases of FSS, three patients had recurrence. There was one mortality during this study period. The median follow up period was 44 (14 - 90) months. Progression free survival (PFS) was 37.41 months and overall survival (OS) was 44 months. The OS rate was 94.45%.

| Variables | Frequency (%) |
|---|--------------------|
| Mean age at diagnosis in years (±SD) | 24.36 ± 4.4 |
| Median follow up period in months (IQR) | 44 (14- 90) months |
| Marital status | |
| Unmarried | 20(55.55%) |
| Married | 16(44.45%) |
| Parity | |
| Nulliparous | 23(63.89%) |
| Para 1 | 11(30.56%) |
| Para 3 | 2(5.55%) |
| Presenting complaints | |
| Pain abdomen | 20(55.55%) |
| Abdominal distension | 7(19.44%) |
| Incidental findings | 5(13.88%) |
| Abdominal mass | 4(11.11%) |
| Tumor size | |
| < 10 cm | 13(36.11%) |
| 10-20 cm | 12(33.33%) |
| >20 cm | 11(30.55%) |
| CA 125 value (U/mL) | |
| < 35 | 15(41.67%) |
| >35 | 21(58.33%) |
| Optimal cytoreduction | |
| Yes | 35 (97.23%) |
| No | 1(2.77%) |
| Histological types | |
| Mucinous carcinoma | 12(33.34%) |
| Borderline serous | 8(22.23%) |
| Serous carcinoma | 8(22.23%) |
| Borderline mucinous | 5(13.89%) |
| Endometrioid carcinoma | 2(5.56%) |
| Clear cell carcinoma | 1(2.78%) |
| FIGO stage | |
| I | 27(75%) |
| III | 8(22.23%) |
| IV | 1(2.78%) |

Table 1: Clinical and pathological features of the study population (n = 36).

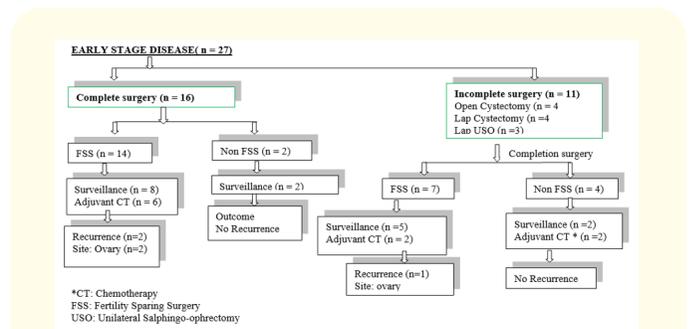


Figure 1: Treatment and outcome pattern in early stage EOCs.

Out of 27 cases of early stage diseases, 11 had incomplete surgery done outside which underwent completion surgery in our center. Two patients who had completed the family underwent non FSS. Figure 1 shows the different methods of treatment received and outcomes.

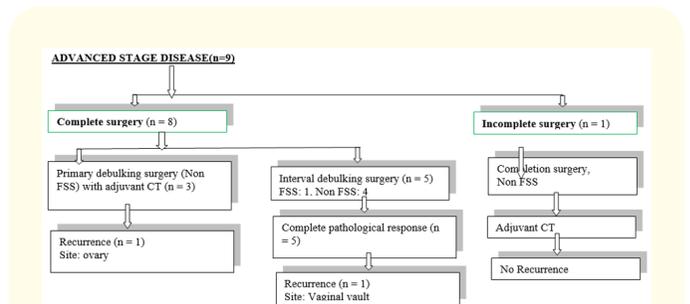


Figure 2: Treatment and outcome pattern in advanced stage EOCs.

Among nine cases of advanced stage diseases, one patient had incomplete surgery done outside. Patient with vaginal vault recurrence underwent surgical excision of metastatic lesion followed by second line therapy. Figure 2 shows the various methods of treatment received.

| Variables | Frequency (%) |
|---|---------------|
| Median time of recurrence (range) in months | 34.8 (5-77) |
| Stage | |
| Stage IA | 2 (40%) |
| Stage IC | 1(20%) |
| Stage IIIC | 2(40%) |

| | |
|---|--------|
| Histological types | |
| Borderline mucinous | 1(20%) |
| Mucinous carcinoma | 1(20%) |
| Serous carcinoma | 1(20%) |
| Papillary serous carcinoma | 2(40%) |
| Fertility sparing surgery | 3(60%) |
| Non Fertility Sparing surgery | 2(40%) |
| Type of first surgery | |
| Incomplete (ovarian cystectomy) | 1(20%) |
| Complete staging surgery | 4(80%) |
| Mode of first surgery | |
| Open | 4(80%) |
| Laparoscopic | 1(20%) |
| Adjuvant treatment after first surgery | |
| Yes | 3(60%) |
| No | 2(20%) |
| Site of recurrence | |
| Ovary | 4(80%) |
| Vaginal vault | 1(20%) |
| Treatment of recurrence | |
| Secondary cytoreductive surgery with chemotherapy | 4(80%) |
| Excision of metastatic lesion | 1(20%) |
| Outcome | |
| Disease free | 4(80%) |
| Mortality | 1(20%) |

Table 2: Clinical characteristics, treatment and outcome of patients with recurrence (n = 5).

| Variables | Frequency (%) |
|---|---------------|
| Resumption of menstruation within one year of completion of treatment | 16 (72.73%) |
| Desirous of pregnancy | |
| Yes | 14(63.64%) |
| No | 8(36.36%) |
| Conception | 11(78.57%) |
| Pregnancy outcome | |
| Live Birth | 9(81.82%) |
| Abortion | 2(14.28%) |

Table 3: Reproductive outcome among patients with FSS (n = 22).

Discussion

EOC is considered as one of the most lethal gynecological malignancies due to vague clinical presentation and advanced stage of disease at presentation. The age adjusted incidences of EOC was 3/100,000 in women younger than 30 years of age [6]. In another study, 1.1% of patients with epithelial ovarian cancer were ≤ 25 years, 4.1% were ≤ 30 years and 13.9% to 17% were ≤ 40 years [7]. There is an increasing trend of EOCs in young women which may be due to better awareness of the disease and improvement in social health.

EOCs in older patients usually present with nonspecific and vague symptoms in late stage of disease. However, younger patients present at early stage with specific symptoms. The common early manifestation of EOCs in young women is a self-palpable or asymptomatic abdominal mass [8]. The exact reason for such difference is not known.

The most common histological type is mucinous carcinoma followed by borderline serous and serous carcinoma. However, these findings are contradictory from previous studies which showed serous carcinoma as the most common histological type followed by mucinous cystadenocarcinoma [8-10].

The EOCs in young patients present in early stage of disease. In this study, 27 (75%) patients presented in early stage of disease. This result is similar to the other studies [6,7]. Chan., *et al.* [11] found that 89.37% of patients less than 30 years with EOCs presented in early stage of disease.

Many studies support the fact that FSS is oncologically safe in stage IA and IC disease and there were no significant differences in oncologic outcome between radical surgery and FSS because the poorest survival observed is related to the natural history of the disease [12-15].

The recurrence rates after FSS vary from study to study ranging from 12.95% to 27.78% [15-18]. However, Park [16] performed FSS in 12 cases of early stage malignant EOCs without recurrence. The recurrence rate after FSS in this study is (13.63%, 3/22).

For advanced stage disease, FSS with complete surgical staging has been performed in few patients but with high recurrence rates [18-22]. Hu [23] performed FSS in 12 cases of advanced stage ovar-

ian cancer (one stage II, four stage IIIA and seven stage IIIC) with high recurrence rate (66.67%,8/12). Ditto 2015 [15] also found the high recurrence rate after FSS for advanced stage disease (85.71%, 6/7). However, Raspagliesi [24] performed FSS in seven patients without recurrence. In this study, one patient with advanced stage disease underwent FSS and there is no disease recurrence.

Tang Li [8] found that for Stage IA disease, the 2- and 5-year survival rate was 86% and 82% respectively and concluded that young women mostly have early stage disease and have good prognosis even with FSS.

EOCs in young women have good prognosis that may be due to early stage at presentation, early symptomatology, improved response to paclitaxel/platinum-based chemotherapy and high success rate of cytoreductive surgery in young patients. The overall survival after 38 months of follow up was 95.4% and recurrence-free survival 84.6% [20]. Several studies have mentioned age as an independent prognostic factor for EOCs [25,26].

Among 22 patients who underwent FSS, 14 were desirous of pregnancy. Nine patients conceived spontaneously, seven patients delivered healthy baby at term and two patients had abortion. The conception rate among patients desirous of pregnancy after FSS is as high as 100% [27]. Satoh, *et al.* [28] performed FSS in 211 patients and the number of patients who desire for child was 84 (40%) out of which 55 (66%) conceived successfully, five with IVF (2.4%) with abortion in 10 (18%) cases. In another study, five out of 13 patients had live births [15]. The fertility rate after FSS in this study was consistent with other published studies [29,30].

As this is a retrospective study, to develop a standard treatment protocol for EOCs in young patients, further prospective studies with large sample size is needed.

Limitations

The limitations of this study are its retrospective nature, small sample size due to rarity of disease and heterogeneous follow-up period.

Conclusion

The management of patients with e EOC in young patients eligible for FSS should be multidisciplinary. EOCs in young patient are rare and unlike in older patient, they are symptomatic in early

stage of disease. They have better survival rates and higher response to first line chemotherapy and even with FSS and complete surgical staging the prognosis is extremely good. Reproductive outcome after FSS is very good with less incidence of recurrence and patient should be informed that radical surgery may not necessarily improve their oncological outcome. However, FSS for advanced disease is highly controversial and needs further investigations.

Conflict of Interest

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

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