Medical and Research Publications
International Open Access

Research Article **Journal of MAR Oncology (Volume 2 Issue 4)**

Epithelial ovarian cancer in adolescent and young adults

Mohana Priya Devarajan[1], Geeta Acharya[1], Premal Atha T S[1], Kiran Abhijit Kulkarni[1], Sivakami Sundari S[2], Vishaka C Bidkar[1], Ramya D R[1]

1. Department of Gynecologic Oncology, St. John's National Academy of Health Sciences, Bangalore, India
2. Epidemiology and Biostatistics, St. John's Research Institute, Bangalore, India

Corresponding Author: Dr. Geeta Acharya, Department of Gynecologic Oncology, St. John's National Academy of Health Sciences, Bangalore, India

Received Date: September 08, 2021

Published date: October 01, 2021

DOI: 10.1027/maroy.2021.0133

Abstract

Objective: *Epithelial ovarian cancer (EOC) is not so common in adolescents and young adults (AYA). Little is known about tumour characteristics and prognosis of EOC in individuals aged 15-39 years. This study was aimed to evaluate the clinic-pathological pattern and survival of AYA individuals with EOC.*

Methods: *A retrospective data review of patients aged 15- 39 years with EOC diagnosed at the Department of Gynaecologic Oncology of St. John's Medical College Hospital, Bangalore, India, and follow-up was done up to 1 year from the last patient included.*

Results: *The mean age of AYA patients were 33 years (21-39 years). Most common presentation was abdominal distension (38.6%) followed by pain abdomen (31.8%). Menstrual irregularities were noted in only 2 (4.5%) patients. Tumour size ranged from 3 to 30 cm and it was unilateral in more than 50% of cases. Of the 44 patients with EOC, 57.8% patients were diagnosed at an advanced-stage EOC. Serous carcinoma was the most common histological type, accounted for 72.7% of the patients followed by mucinous histology (13.6%). Almost 70% of patients had high grade tumours of all histological types. Among 44 patients, 31 underwent primary surgery and 13 received neoadjuvant chemotherapy. The mean progressive free survival (PFS) and overall survival (OS) was 5.8 years and 6.7 years respectively. There was a statistical difference in PFS by primary mode of treatment but no difference in PFS by stage or grade of disease. There was also no statistical difference in OS by stage, grade, or mode of treatment.*

Conclusions*: AYA with EOC are mostly diagnosed at an advanced staged. They are commonly high-grade serous adenocarcinoma and unilateral tumours. Fertility sparing surgery can be considered in low grade and early stage EOC.*

Keywords*: survival, fertility, AYA, ovarian cancer*

Abbreviations*:*

EOC- Epithelial Ovarian Cancer

GLOBOCAN- Global Cancer Observatory

AYA- Adolescent and Young Adults

ECOG PS- Eastern Cooperative Oncology Group Performance Score

FIGO- The International Federation of Gynecology and Obstetrics

s/p BSO±TAH- post Bilateral Salphingo- Oophorectomy ± Total Abdominal Hysterectomy

Introduction

Epithelial ovarian cancer **(**EOC**)** is common in postmenopausal women with less than 20 % incidence in women below 40 years of age **(**1**)**. It has high mortality rate among gynaecologic cancers and it is the seventh most common cancer in females globally **(**2**)**. National cancer institute grouped individuals aged 15 to 39 years at the time of initial cancer diagnosis as adolescent and young adults **(**AYA**) (**3**)**. AYA patients with EOC comprise a special subset as some of these patients may desire future fertility and hormone function preservation. Studies have shown fertility sparing surgery **(**FSS**)** to be safe and effective method in young patients who have undergone a thorough staging surgery in grade 1 or 2, stage IA and IC ovarian cancer **(**4**)**. patients who have undergone a thorough staging laparotomy in grade 1 or 2, stage 1A and 1C tumour. Little is known about malignant epithelial ovarian tumour in AYA group. This study analysed clinico-pathological pattern and survival outcome based on stage, grade of tumour, residual disease and primary modality of treatment of 44 AYA patients with epithelial ovarian cancer.

Materials and methods:

The study was done as a retrospective data review of patients aged 15- 39 years with epithelial ovarian cancer diagnosed at Gynaecologic Oncology out patient department of St. John's Medical College Hospital, Bangalore, India, and follow-up was done up to 1 year from the last patient included.

Patients were identified through the electronic medical records. All the patients fulfilling our inclusion criteria were contacted by phone. Oral consent was obtained to include the patient for study. If patient had expired, the details of death were obtained from a relative. The patient's demographic details, clinical presentations, histological features, treatments and survival outcome data were collected mainly by reviewing the electronic medical records. This study was approved by our Institutional Review Board.

Inclusion Criteria:

- Patients aged 15-39 years with primary epithelial ovarian cancer at the time of diagnosis

- Completion surgery at our centre for patients incompletely staged elsewhere

Exclusion Criteria:

- Patients ≥ 40 years and < 15 years of age

- Borderline ovarian tumour

- Metastatic ovarian disease

-Those who did not have epithelial ovarian cancer in final histology

Statistical Analysis

Kolmogorov-Smirnov test was used to test the normality. Continuous variables were presented with mean and Standard deviation or median and Inter quartile range as appropriate. Categorical variables were reported with frequency and percentage. Kaplan Meier method was applied to find the mean survival and recurrence time. Tarone ware test was used to examine the significance of difference in survival between groups. The results were considered statistically significant at the level of alpha <0.05 in all analysis. Statistical analysis was performed using IBM SPSS Statistics 25.0.

Results:

Between 2012 and 2019, 44 patients aged 15- 39 years were diagnosed with malignant epithelial ovarian tumour and fulfilled our eligibility criteria. The baseline characteristics, histopathological pattern and treatment details of the study patients are summarized in Table 1.

The mean age of AYA patients with EOC was 33 years and 88.7% of the patients were in a good performance status **(**ECOG PS 0,1**)**. Most common presentation was abdominal distension **(**38.6%**)** followed by pain abdomen **(**31.8%**)**. Menstrual irregularities were noted in only 2 **(**4.5%**)** patients. Around 70% of the patients were parous women and 26.7% were nulliparous, out of which 5 patients were evaluated for infertility. Tumour size ranged from 3 to 30 cm and it was unilateral in more than 50% of the patients. The median CA 125 was 1269.1 IU/L **(**ranged between 10.5- 5000 IU/L**)**. Of the 44 patients with EOC, 57.8% patients were diagnosed at an advanced-stage EOC **(**stage III and IV**)**. Serous carcinoma was the most common histological type, accounted for 72.7% of the patients followed by mucinous histology **(**13.6%**)**. Almost 70% of patients had high grade tumours of all histological types. Nine of the 44 patients **(**20.45%**)** were incompletely staged elsewhere and underwent completion surgery at our centre. Out of 9 incompletely staged patients, 5 patients were diagnosed during diagnostic laparoscopy performed for infertility evaluation.

Majority of the patients **(**70.4 %**)** underwent upfront surgery and remaining 29.6% patients received neoadjuvant chemotherapy **(**NACT**)**. Almost all patients who underwent primary surgery received 5-6 cycles of adjuvant chemotherapy except ovary confined disease in mucinous and low-grade serous tumours. Around 50% of the patients received adjuvant chemotherapy on post-operative day 11. Only 2 patients in the adjuvant setting received cyclophosphamide and cisplatin due to cost factor whereas rest all patients received paclitaxel 175 mg/m2 and carboplatin AUC 6 three weekly regimen which is the standard of care for epithelial ovarian cancer. Nearly 90% of the patients underwent interval debulking surgery **(**IDS**)** after 3 cycles of NACT with paclitaxel and carboplatin but 27.2% patients received only 1 or 2 adjuvant cycles due to chemotherapy induced toxicity.

Optimal cytoreduction achieved in 92.8% of patients and suboptimal resection in 7.1% of patients. Out of 12 nulliparous women, only one patient with mucinous ovarian cancer confined to one ovary underwent fertility sparing surgery (FSS) and remaining 11 patients did not undergo FSS as they were diagnosed with either advanced ovarian disease or high grade serous ovarian cancer. Out of 44 patients, 29 (65.9%) patients completed treatment without any delay.

Survival and recurrence based on variables like stage, grade of the disease and primary modality of treatment were analysed separately. The mean progressive free survival (PFS) and overall survival (OS) was 5.8 years and 6.7 years respectively. There was no significant difference in PFS or OS when compared by stage of the disease (p=0.146 & p=0.181) or grade of tumour (p= 0.099 & p= 0.071) respectively as depicted in figure 1-4. There was a significant difference in PFS but not in OS when compared by primary mode of treatment (p= 0.014 & p=0.078) as depicted in figure 5 &6.

Discussion

Cancer literature have revealed that AYA oncology patients did not demonstrate the improved outcomes observed in children and older adults (age > 40 years). The main reasons for poor outcomes are differences in disease and host biology, different treatment approaches, delayed diagnosis, poor adherence to therapy, psycho social, economic and fertility issues and exceedingly low participation in clinical trials (5). According to Age-Specific SEER data, breast cancer (21.7%) is the most common cancer in AYA female population followed by thyroid cancer (19.1). There is a scarce documentation of the pattern and characteristics of EOC in AYA group in the literature as EOC is common in the postmenopausal age group (6).

The common clinical presentation in our study was abdominal distension (38.6%) followed by pain abdomen (31.8%) whereas abdominal pain was the common presentation in two Indian studies which had analysed EOC in young women (7,8)

More than half of our patients (57.8%) were diagnosed at an advanced stage of disease which is similar to Wangdi et al., study (7). Around 70 % of our AYA patients had high grade tumours of all histological types but it was of low grade and early stage in most of the similar studies (1, 9). Serous carcinoma was the most common histological type as mentioned in similar other studies (1,7)

Wangdi et al., reported that the paucity of information, availability and affordability of health services and lack of knowledge were the factors that contribute to advanced stage disease in young women (7). Lack of preparedness, poor acceptance, lack of knowledge and improper referral are the probable contributing factors that lead to delayed diagnosis in our patients.

Nine out of 44 AYA patients operated elsewhere had incomplete surgery in which 55.5% of patients had diagnosed during diagnostic laparoscopy performed for infertility evaluation. The usual reasons for

incomplete surgery/staging are improper preoperative imaging, lack of awareness, technical difficulty and lack of adequate facility such as frozen section. In our centre, all patients who were incompletely operated elsewhere underwent upfront re-intervention. Seven out of nine incompletely operated patients were upstaged and they all had fallen into advanced EOC stage. Wangdi et al., reported that they preferred to give NACT followed by interval surgery to patients with incompletely operated advanced stage disease **(**7**)**. Nicolae et al., found that the patients who had undergone incomplete procedure, NACT followed by IDS was associated with survival benefit as compared to upfront re-intervention **(**10**)**.

Almost all patients who underwent primary surgery received 5-6 cycles of adjuvant chemotherapy without cycle delay and almost half of the patients had received on eleventh postoperative period but 27.2% of NACT patients have not completed adjuvant chemotherapy after interval surgery due to chemotherapy induced toxicity and poor compliance.

The mean PFS and OS in our study was 5.8 years and 6.7 years respectively and our outcome is superior than Lalrinpuii et al., study **(**8**)**, where the mean PFS in young epithelial ovarian cancer was 3.8 years. Wangdi et al., found overall 2-year disease free survival as 69% which was lower than the previous similar studies **(**7,11**)**. The reasons for better outcome in our study could be optimal cytoreduction that had achieved in 92.8% of our patients, re- surgical intervention in incompletely staged patients, initiation of adjuvant chemotherapy within 2 weeks of surgery and adherence to treatment.

FSS was offered to only one patient with stage IA, grade 1 mucinous ovarian cancer and remaining 11 patients who had not completed treatment, had either advanced ovarian disease or high-grade ovarian cancer.

We could find better PFS in patients who underwent primary surgery but there was no statistical difference in overall survival when compared with NACT patients. According to Tang et al., two and five-year survival rates were 86.0% and 82.0%, respectively and they had reported that residual disease and pathological grade as independent prognostic factors in young EOC patients **(**12**)** but we couldn't find any such association in our study. It might be due to small sample size.

Conclusion:

Most of our AYA patients were diagnosed at an advanced stage disease with high grade serous histology. Fertility-sparing surgery should be considered in AYA seeking future pregnancy in selected early stage and low-grade disease. Studies on molecular testing and its impact on survival are warranted to predict better survival in these special group.

References

1. Duska, Linda R., et al. "Epithelial ovarian carcinoma in the reproductive age group." Cancer 85.12 (1999): 2623-2629

2. Sung, Hyuna, et al. "Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries." CA: a cancer journal for clinicians 71.3 (2021): 209-249.

3. Coccia, Peter F. "Overview of adolescent and young adult oncology." (2019): 235-237

4. Schilder, Jeanne M., et al. "Outcome of reproductive age women with stage IA or IC invasive epithelial ovarian cancer treated with fertility-sparing therapy." Gynecologic oncology 87.1 (2002): 1-7

5. Ferrari, A., et al. "Adolescents and young adults (AYA) with cancer: a position paper from the AYA Working Group of the European Society for Medical Oncology (ESMO) and the European Society for Paediatric Oncology (SIOPE)." ESMO open 6.2 (2021): 100096

6. Howlander, N., A. M. Noone, and M. Krapcho. "National Cancer Institute. SEER Cancer Statistics Review, 1975–2015." (2018)

7. Wangdi, Tsering, et al. "A Clinico-pathological Analysis of Women with Epithelial Ovarian Cancer in 20–40 Years Age Group." Indian Journal of Gynecologic Oncology 15.3 (2017): 1-5.

8. Lalrinpuii, Eileen, et al. "Ovarian cancer in young women." Indian journal of surgical oncology 8.4 (2017): 540-547.

9. Plaxe, S. C., et al. "Profiles of women age 30-39 and age less than 30 with epithelial ovarian cancer." Obstetrics and gynecology 81.5 (Pt 1) (1993): 651-654.

10. Bacalbasa, Nicolae, et al. "Initial incomplete surgery modifies prognosis in advanced ovarian cancer regardless of subsequent management." Anticancer research 35.4 (2015): 2315-2320.

11. Chan, J. K., et al. "Ovarian cancer in younger vs older women: a population-based analysis." British journal of cancer 95.10 (2006): 1314-1320.

12. Tang, Li, et al. "Clinical characteristics and prognosis of epithelial ovarian cancer in young women." Ai zheng= Aizheng= Chinese journal of cancer 27.9 (2008): 951-955.