Original Article

The Outcome Of Ovarian Cancer Patients In Single Institute Duhok

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DOI: 10.47750/pnr.2023.14.S02.333

Abstract

Background and objectives: The most common gynecological malignancy in Kurdistan is ovarian cancer with high morbidity and mortality. Ovarian cancer patient usually diagnosed at late stage because they have non-specific symptom at early stages. Most ovarian cancer patient treated with surgical operation followed by adjuvant- chemotherapy.
Methods: In this retrospective (cohort) study, a total 155 patient treated at Azadi cancer center in Duhok between May 2015 and April 2021. Clinico-pathological information data and case registration exanimated to assess the management outcome, stage of disease, histo- pathology of the tumor and overall -survival (OS) rate of patients.

Results: the mean age was 48.5 years (range 12-89 years). The most common histology subtype was epithelial ovarian cancer. In this study patient with late stage disease were more common than early stage ovarian cancer patient, 56% and 44% respectively. Median OS of all patient included in this study is 28 months (95% CI of 24-34 months). Patients with early stage disease (stage I and stage II) and had better outcome to patient with advance stage disease (stage III and IV) (P=0.006). Patients treated with upfront surgery after diagnosis had uppermost OS with a median overall survival, 31 months (95% confidence interval of 27-39 months) compared to patient treated with neoadjuvant treatment or first line treatment with OS 21 months (95% confidence interval of 12-30 months) and 5 months (95% confidence interval of 1-31 months) respectively (P= 0.0137).

Conclusions: Ovarian cancer has an improved prognosis when diagnosed at early stages. Surgery is the main stay of the treatment, followed by proper chemotherapy.

Keywords: ovarian cancer, chemotherapy, overall survival.

Introduction:

Ovarian cancer is the fourth leading cause of mortality in cancer patients and about one third of women are diagnosed with potentially curable disease at presentation. The majority of tumors arise from surface epithelial cells; serous ovarian cancer is the most common among them. Other cancers arise from the germ cells and the stromal cells. [1, 2]

Patients with ovarian cancer typically have vague symptoms. Possible signs and symptoms include ascites-related significant abdominal swelling, newly developing meteorism, changes in bowel habits, and generalized abdominal discomfort[2]. At time of diagnosis, it is very important to identify appropriate staging to achieve proper cytoreduction at the time of surgical intervention. [1, 3, 4]

Patients with ovarian cancer present with non-specific symptoms. Possible symptoms range from diffuse abdominal complaints, newly occurring meteorism, changes in bowel habits, and unexplained weight loss to massive abdominal swelling due to ascites. [5]

The cancer outcome is significantly higher when the disease is diagnosed at an early stage, but unfortunately there is no accurate non-invasive diagnostic test to detect the disease at an early stage [6]. Trans-vaginal ultrasound is one of the best diagnostic tests, blood tests can detect tumor markers in the blood, CA125 can be elevated in patients with epithelial ovarian cancer (EOC), but it is not specific, other tests that may help in staging the disease include diagnostic laparoscopy, CT scan and/or MRI of the pelvis. [2]

Several aspects determine the prognosis of ovarian cancer; genetic factors are the most important among them, approximately 10-15% of genetic ovarian cancers results from mutation of the BRC gene. Most ovarian cancers are heterogeneous in origin. While infertility is connected with an elevated risk of ovarian cancer, breastfeeding has not been proven to reduce the risk of ovarian cancer [2, 7].

There is no standard treatment for ovarian cancer. The treatment methods are dependent by the stage of the disease and the nature of tumor. Current treatment options include debulking surgery, chemotherapy, radiation therapy and targeted therapy. The treatment of peritoneal disease best achieved by intraperitoneal chemotherapy instillation [2, 7-9].

Material and Methods

This study was a retrospective cohort study using secondary data from medical records of patients. A total 155 patient treated at Azadi cancer centre in Duhok between May 2015 and April 2021. Patients without any approved documents for ovarian cancer excluded, such as peritoneal carcinomatosis with unknown primary origin. Additionally patient with lost for follow up were also excluded from this study.

Patients were first assessed for gynecologic examination, imaging tests (especially MRI and CT scan), and tumor markers (CA125 and CA19.9), According to these evaluations, patient characterized into early stage disease and advance stage disease. TNM staging was used to sub classify patient into four stages (I, II, III and IV). Early-stage cancer patient (stage I and stage II)and young age, fertility-preserving surgery done with unilateral oophorectomy. On other hand cases, either old age or who had completed family had total abdominal hysterectomy and bilateral- salpingoophorectomy (TAH BSOO). Epithelial ovarian cancer patient with advance disease (stage III and IV) had neoadjuvant chemotherapy inform of Paclitaxel 175 mg/m2 and carboplatin were given in 6 cycles over the course of 3 weeks (area under the curve: 5-6) as the standard of care. This followed by debulking surgery aiming at completed excision (TAH BSOO, pelvic and par aortic lymph-adenectomy, and radical infra-colic omentectomy). All patient included in this study follow up closely for the outcome to evaluate the response to treatment and classify tumor response in stable disease, completed response (CR), NO response (NR),and progressive disease (Recurrence or metastasis disease). The patients who developed recurrence have received second line treatment.

The Kaplan-Meier used to estimate overall survival of ovarian cancer patient.In addition to survival outcome according stage of disease, presence of surgical margins and malignant ascites. Statistical computing performed using SPSS. The Log Rank (Mentel-Cox) test was used to analyze the data by SPSS version 17 (SPSS Inc. Chicago Illinois, USA). The p-value for this study's significance threshold was <0.05.

Results:

The study consisted of 155 cases with a median- age of 48.5.0 years (range 12-89).The clinic-pathologic characteristic of the patients show in **Table 1**. The most frequent histological type was serous epithelial cancer (77%). There were 55 cases of progression and 27 deaths at time of analysis Table 1.

Table 1: clinicopathological patient characteristics

Diagnostic methods (n=155)	**No**	**%**
Age (12-89 years) Mean (SD)	48.5 (18.5)	
Mortality Alive Dead	 128 27	 83 17
Front treatment First line chemotherapy Neoadjuvant chemotherapy Surgery resection followed by Adjuvant chemotherapy	 7 44 104	 6 27 67
Ascitic fluid result Negative Ascitis fluid Positive Ascitic fluid (malignant)	 96 59	 62 38
Histopathology Epithelial Ovarian cancer Serous Epithelial Ovarian cancer Non serous Epithelial Ovarian cancer* Germ cell cancer Dysgerminoma Embryonal carcinoma Yolk Sac Sex cord –Stroma	 119 20 16	 77 13 10
TNM I II III IV	 55 13 76 11	 36 8 49 7
Type of surgery Cytology aspiration Laparoscopy excisional Biopsy Laparoscopy Tumor excision TAH-BSO/open surgery	 13 13 45 84	 8 8 29 55
Chemotherapy Bleomycin +Etoposid + Cisplation (BEP) Taxol + carboplatine Taxol+carboplatine + avastine Other regimen protocol	 18 101 32 4	 12 65 21 2
*Non serious Epithelial Ovarian cancer (Mucinous , Endomatriod , clear cell cancer , Transitional cell cancer		

Fifty-six patients (56%) had advance disease and Forty-four patients had early stage disease (44%). Median OS of all patient included in this study is 28 months (95% CI of 24-34) (Figure 1). A statistically significant difference between those with early-stage cancer and OS outcomes was found. (stage I and II) and case with advance stage disease (stage III and IV) (P=0.006). For cases with early stage(I,II) disease, the mean OS

was 32 (months) and 52 for stage I and II respectively, while the OS rate for patients with late stage disease had an average OS 23 months and 9 months respectively (Table 1, Figure 2).

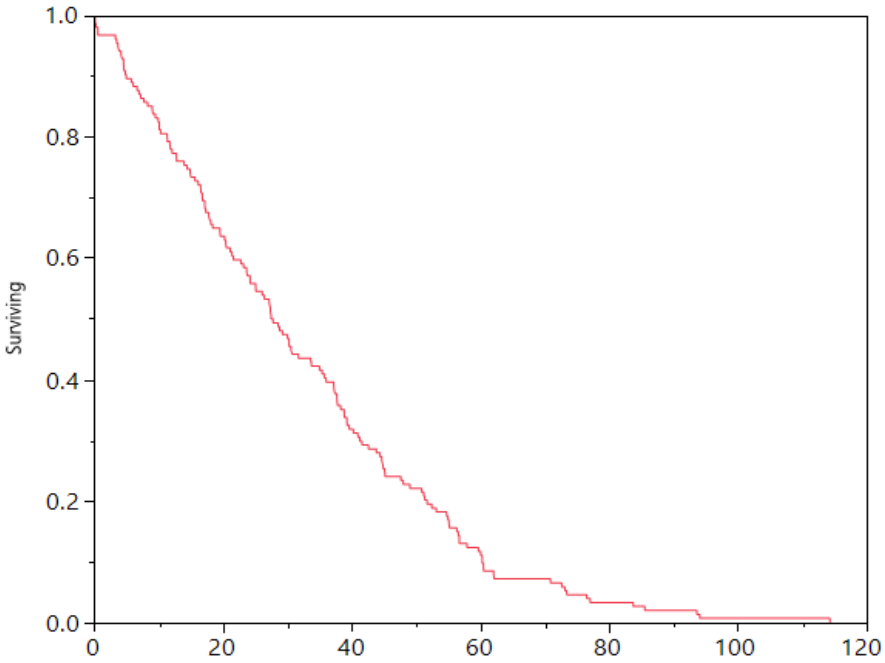

Figure 1. Overall survival in patients with ovarian cancer treated in Duhok city/Kurdistan/Iraq. Median OS of all patient included in this study is 28 months.

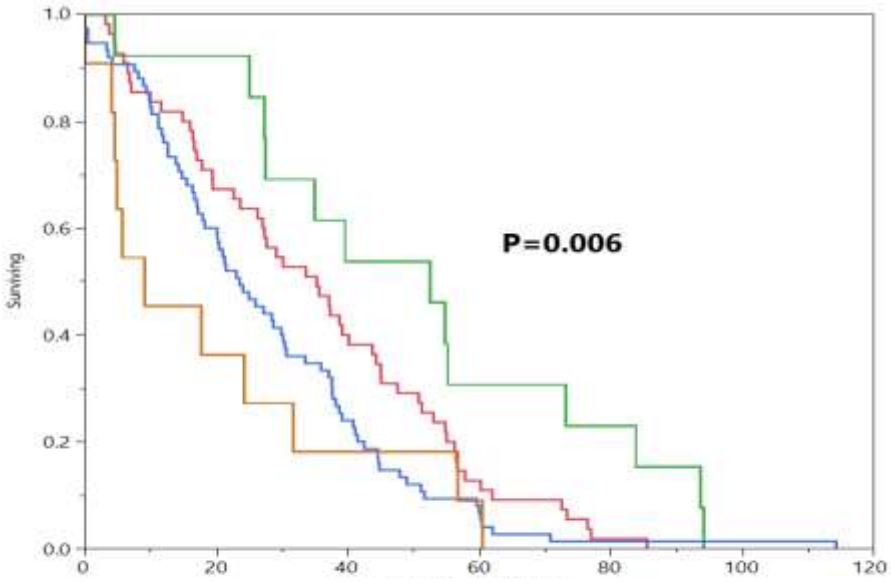

Figure 2. Overall survival in patients with ovarian cancer by stage of disease at time of first presentation.

Patient treated with upfront surgery after diagnosis had highest OS with a median overall survival, 31 months (95% confidence interval of 27-39 months) compared to patient treated with neoadjuvant treatment or first line treatment with OS 21 months (95% confidence interval of 12-30 months) and 5 months (95% confidence interval of 1-31 months) for first line chemotherapy respectively (P= 0.0137) (Figures 3). Actually, the overall survival varied substantially depending on the extent of the surgical resection. The OS of cases who had positive margin after surgery had worse outcome compared to those with negative margins with OS of 20 months (95% confidence interval of 12-27 months) and 34 months (95% confidence interval of 27-39 months) respectively (Figures 4).

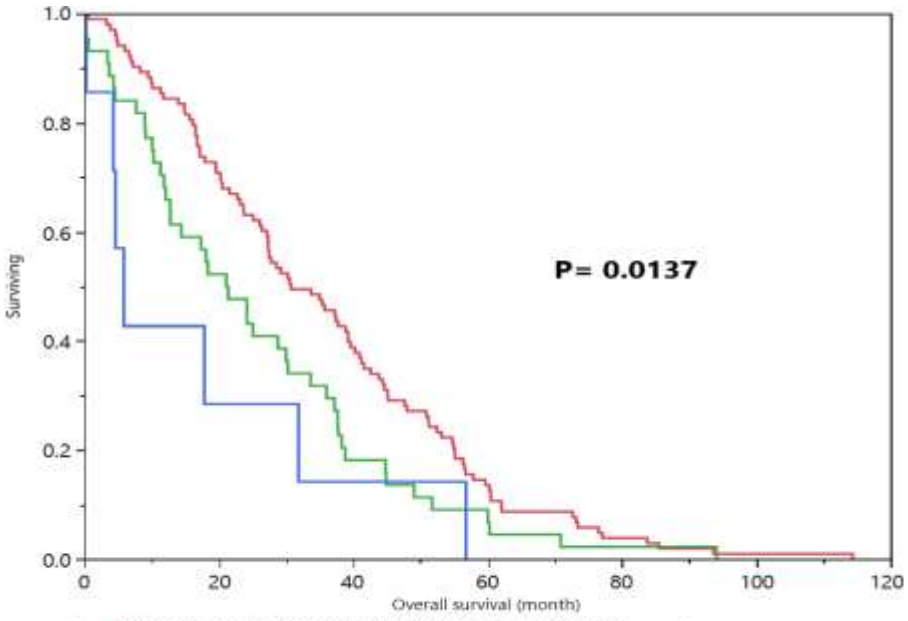

Figure 3. Overall survival in patients with epithelial ovarian cancer by type of first line treatment.

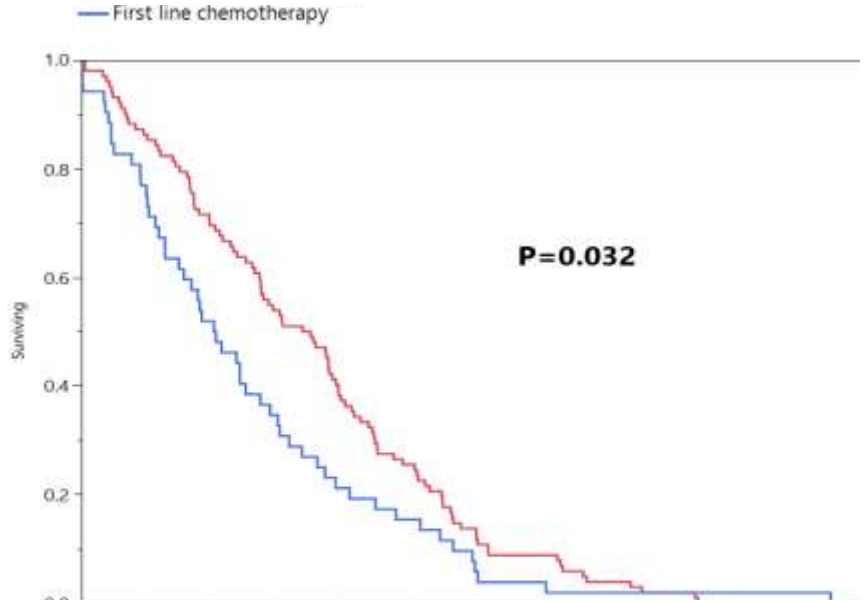

Figure 4. Overall survival in patients with ovarian cancer by identifying margin after surgery.

Although maximum duration of OS achieved in ovarian cancer patient with negative ascites for malignant cells, whereas a minimal OS duration was seen in cases with positive ascites with OS of 30 months (95% confidence interval of 26-39 months) and 23 months (95% confidence interval of 16-31 months) respectively but this was statistically non-significant (P= 0.05) (Figures 5).

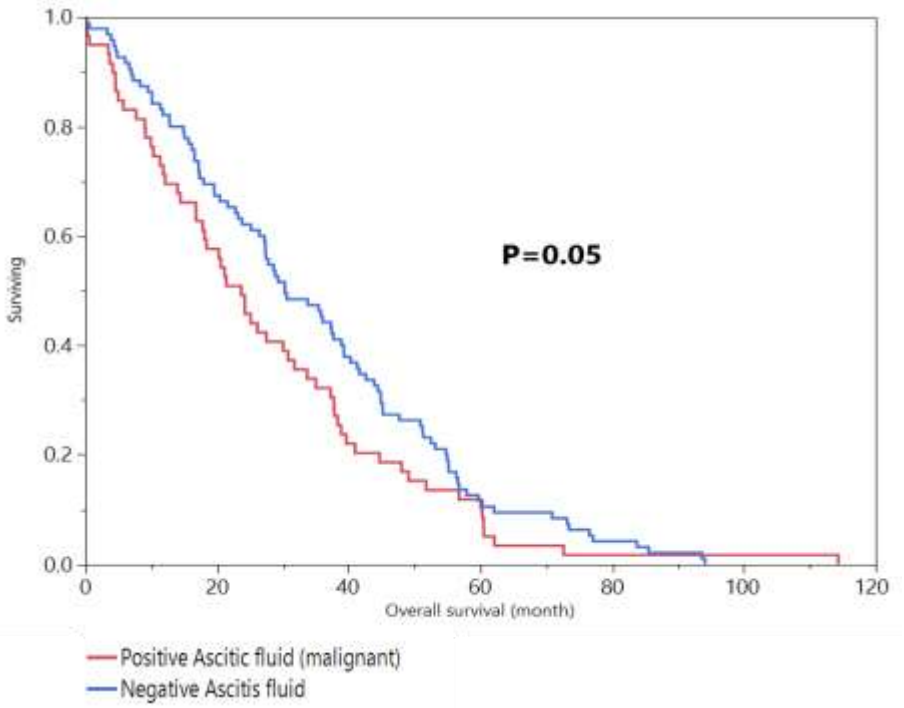

Figure 5. Overall survival in patients with ovarian cancer with and without positive ascites.

Discussion:

The incidence of cancers as general is increasing all over the world including ovarian cancer. We have previously showed In Kurdistan/Iraq, ovarian cancer is the most prevalent gynecologic malignancy. [10]. In current study on 155 patient shows that a most prevalent ovarian cancer histologic subtype found in Duhok city is serous adenocarcinoma this is in keeping with most published studies on ovarian cancer[2, 11, 12].

The majority (>80%) of cases of ovarian cancer are diagnosed in women over the age of 50, who are primarily older, postmenopausal women. Despite the fact that there are numerous established risk factors, the underlying etiology of ovarian cancer is still unclear. The lifetime risk of ovarian cancer for women appears to be significantly influenced by their reproductive history. In current study, the majority of cases who diagnosed with OC were ranging between 40 and 70 years. The diagnosis made based on biopsy histopathology results, tumor markers are not used for the diagnosis but a sharp rise after treatment may indicate recurrence of the disease. In our study most cases were diagnosed based on tissue biopsy obtained by laparoscopic or open surgery. The most common histological type was epithelial type; other histological subtypes are germ-cell tumors and sex-cord stromal tumors. Most our patients diagnosed at advance stages, while other diagnosed at early disease. The five-year survival percentage for OC patients with TNM Stages III to IV (tumor in the pelvis or other areas of the abdomen) is less than 40%, but the rate for early stages, TNM Stages I to II, is substantially higher, at more than 80%. Because of this, it's crucial to offer a diagnosis as soon as feasible. In our study, about 56% of patients diagnosed as stage I and II, while 45% diagnosed in stage III and IV of the disease [4, 5].

Depending on the resources available and the stage of the disease, the quality of therapy and adherence to treatment criteria vary substantially, if patient treated according to guidelines, they might have better survival. However, in our locality most cases are diagnosed at advance disease therefore they need to have NAC to downstage the disease followed by surgery aiming at complete excision.

Numerous studies contrast OC patients getting NAC with those not receiving NAC. The survival rate for patients treated with primary surgery was found to be greater than that for patients who received surgery following NAC, according to a newly published Turkish retrospective cohort research in which 99 individuals were reviewed. In a study, by Ren and his colleagues, reported lower OS in the neo-adjuvant group in a 408 patient trial.. Other studies showed improved survival in cases treated with NAC [(13)].

These groups, however, are not comparable enough to be compared. Patients who have been anticipated to be candidates for ideal surgery are scheduled for primary debulking surgery. Patients who are not candidates for main optimum debulking surgery are postponed till after NAC for interval debulking surgery. This suggests that individuals who were regarded "operable" were chosen for surgery up front, whereas those who got NAC seemed to not be candidates for full excision. Since these two cohorts have distinct disease burdens and biologies, which are anticipated to be worse in patients who are not candidates for primary surgery, one cannot make any judgments regarding the differences in outcomes. Another hypothesis is that NAC impairs intraoperative assessment and raises the likelihood of complications. Because of how chemotherapy affects the tissue, the tumoral region may be skipped and the difficulty of removing possibly resectable tumor tissues may have a harmful effect. [(14, 15)] .

Another theory is that the first use of NAC causes the majority of tumor cells to die off and eventually causes the formation of chemotherapy-resistant tumor cells in stem cell colonies. As evidenced by several studies, NAC gradually raises the risk of platinum resistance. [(16-18)].

The largest independent factor that impacts the prognosis after disease stage is residual tumor following surgery. 50% to 85% of patients with advanced ovarian cancer who have surgery by experts in gynecological oncology can obtain a residual tumor of less than 1 cm. Therefore, total tumor excision must be the goal of every surgery. [(5, 19, 20)].

The presence of ascites at time of diagnosis is sign of poor prognosis. In this study, patient with positive ascites had worse outcome compared to patient with negative ascites. This is consistent with other literature results. Indah Nur Damayanti and his colleagues showed significant better three-year OS outcome of patient with negative ascites. Ascites and survival may be related, according to several researches. Patients with epithelial ovarian cancer who also had ascites had a 3.5 times higher probability of dying than those who did not have ascites.

The present study has some limitations such as it include all histological subtype of ovarian cancer treated in Duhok city as well as its retrospective design. In furthermore, patient underwent surgery that is optimal for standard cyto-reductive operation but undergoes sub-optimal operation with certain limitation of surgical approach. Even after NAC, some individuals may be unable to have optimum surgery. and may refuse surgery after having good response.

Conclusion:

This review investigated at a group of ovarian cancer patients who were treated with various methods based on their stage of disease and histological subtype. Ovarian cancer has an improved prognosis when diagnosed at early stages. Surgery is the main stay of the treatment, followed by proper chemotherapy. The aim of treatment is to achieve complete excision and proper follow up.

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