Research Report

Early-Stage epithelial ovarian cancer: Predictors of survival

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A B S T R A C T

Background: One fifth of patients with epithelial ovarian cancers (EOC) present at an early stage (FIGO stage I & II). However, there is scarcity of literature on the outcomes and its predictors. The aim of the study was to assess relapse free survival (RFS), overall survival (OS) and its predictors in early stage EOC.
Patients and Methods: In this retrospectively study, we included all patients with early-stage EOC diagnosed between January 2010 and December 2018. Patients with synchronous malignancies were excluded. Clinical profile, clinico-pathological characteristics and treatment details were recorded. Patient underwent initial surgery followed by adjuvant chemotherapy in high-risk disease. Patients with stage IC, or stage II or clear cell histology or high-grade histology irrespective of stage/histological subtype were defined as high-risk disease. Fertility sparing surgery (FSS) [unilateral salpingo-oopherectomy with complete surgical staging] was performed in patient willing to preserve fertility. Primary objective was to assess RFS and OS in all patients with early stage EOC. Secondary objectives were to assess RFS and OS in early stage EOC with high-risk disease, predictors of RFS and OS, and outcomes of FSS. Survival probabilities were estimated according to Kaplan-Meier and compared by the log rank test. Cox's regression model was used to analyze the significance of various factors affecting relapse free survival (RFS) and overall survival (OS).
Results: 195 patients with early stage EOC were recruited with median age of 47 years (range, 16–80 years). FIGO stage I and stage II were seen in 72 % and 18 % patients respectively. Serous subtype was reported in 58 % and high-grade histology in 66 %. 184 patients (94.0%) underwent optimal staging surgery, including 27 (14%) with fertility sparing surgery (FSS). 133 (91.7 %) of 145 patients with high-risk disease received adjuvant chemotherapy (paclitaxel and carboplatin), while 12 (8.3 %) patients opted to remain on observation. At median follow up of 56 months (95 % CI, 46–64 months), 49 (25 %) patients relapsed [including 3 of 27 (11.1 %) who underwent FSS], 18 patients died of progressive disease, while 31 patients were alive and disease free. Estimated OS at 5 years is 87.6 % (95 % CI 79.9–92.5) and RFS is 73.2 % (95 % CI 64.7–80.0). On multivariate analysis tumor grade was predictive of RFS (HR 2.9, p < 0.04) and OS (HR 9.4, p < 0.02).
Conclusions: This study confirms the excellent outcome for patients with early stage EOC. Histological grade of tumor is a significant predictor of OS and RFS. FSS is feasible in selected patients with early EOC.

1. Introduction

Epithelial Ovarian cancer (EOC) is common gynecological malignancy. Approximately 20 % of patients present with early-stage disease. Following surgery outcome for these patients is very good with five-year survival in the range of 80 % to 93 %, but there is significant risk of relapse in patients with high-risk disease (Berek et al., 2021 Oct; Menon et al., 2021; Torre et al., 2018). As such, role of adjuvant chemotherapy for early EOC has been debated as the earlier trials are flawed by heterogeneous population, inadequate surgery, survival benefit only in certain subsets, use of nonstandard chemotherapy drugs and varying number of chemotherapy cycles.

In International Collaborative Ovarian Neoplasm (ICON) 1 trial, adjuvant chemotherapy demonstrated significant relapse free survival

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(RFS) and overall survival (OS) advantage. While in Adjuvant Chemo-Therapy In Ovarian Neoplasm trial (ACTION) trial, OS benefit was only observed in inadequately staged patients. In both these trials only one third of patients underwent optimal staging surgery and single agent platinum or a combination of cisplatin, adriamycin and cyclophospha-mide was administered as adjuvant therapy in majority of patients (not the current standard of chemotherapy). However, combined analysis of these two landmark trials [International Collaborative Ovarian Neoplasm (ICON) 1 and Adjuvant ChemoTherapy In Ovarian Neoplasm trial (ACTION) demonstrated significant benefit of adjuvant chemo-therapy in early-stage disease with OS difference of 8 % in favor of chemotherapy (82 % versus 74 %, respectively; P = 0.008). Recurrence-free survival (RFS) was also better for patients in the adjuvant chemo-therapy arm (76 % versus 65 %, respectively; P = 0.001) (Colombo et al., 2003; Trimbos et al., 2003; Trimbos et al., 2003 Jan 15). 10 years follow up of ICON1 trial confirmed these results demonstrating benefit of chemotherapy particularly in high-risk disease (Swart, 2007). Furthermore, adequate number of chemotherapy cycles is also debat-able. In GOG 157, high-risk early stage EOC were randomized to three or six cycles of paclitaxel and carboplatin. No OS or RFS difference was observed except in patients with serous histology (constituted only 30 % of the trial population), who benefitted from six cycles of adjuvant chemotherapy.

Among important prognostic factors – age, tumor grade, stage, as-cites, surface tumor, and tumor capsule rupture have been shown to be independent predictor for relapse in early stage EOC irrespective of adjuvant chemotherapy. The relapse rate varies from 10 % to 50 % in different studies due to heterogeneity of population included. e.g. for FIGO stage IC-II – 5 year OS ranges from 60 to 70 % compared to 90 % for stage IA-IB. (Cannistra, 2004 Dec 9; Tropé and Kaern, 2007 Jul 10; Matz et al., 2017 Feb; Hsieh et al., 2019; Wei et al., 2016 Nov 11; Tognon et al., 2013; Bamias et al., 2011 Oct 1; Lheureux et al., 2019 Mar 23).

With excellent survival, the issue of fertility sparing surgery (FSS) in young EOC patients is an important consideration; many of them are unmarried or have not yet completed family. FSS may be considered especially if they have low risk (stage IA or IB with low grade and non-clear cell histology) EOC. (Schuurman et al., 2021 Feb 28; Liu et al., 2020 Apr 15) Recurrence rate after FSS in early EOC varies from 9.9 % for stage IA/IB, 15.4 % in stage IC to 40 % in stage II. (Kwon et al., 2009 Mar) A recent metanalysis found no difference in survival between FSS and radical surgery in stage- I disease. (Schlaerth et al., 2009 Oct). NCCN guidelines also recommend unilateral salpingo-oopherectomy (USO) or bilateral salpingo-oopherectomy (BSO) with uterine preservation for selected stage IA-IIA patients desiring to preserve fertility. (Armstrong et al., 2022 Sep 1).

In the current study, we report long-term outcome and predictive factors for early stage EOC. We also analysed the role of fertility sparing surgery (FSS) and adjuvant chemotherapy regimen in high risk patients treated uniformly with six cycles of paclitaxel and carboplatin.

1.1. Patients and Methods

All women diagnosed and treated for early ovarian cancer at our institution between January 2010 and December 2018 were included in this retrospective study. Patient baseline characteristics, demographic data, clinical features, histopathological profile, serum markers, radio-logic findings, stage, operative procedure, and adjuvant treatment were recorded. Histopathological slides were reviewed in all patients to determine the tumor grade. Grading was done as either high grade or low grade on basis of WHO classification (Hohn et al., 2021). Residual disease after surgery was considered in presence of macroscopic pelvic disease after surgery. Inadequate staging surgery defined if complete surgical staging not performed. All patients were staged according to FIGO (Federation Internationale de Gynecologie et d Obstetrique) 2014 classification (Prat et al., 2014). Primary objective was to assess relapse free survival (RFS) and overall survival (OS) in all patients with early

stage EOC. Secondary objectives were to assess RFS and OS in early stage EOC with high-risk disease, predictors of RFS and OS, and outcomes of FSS. The Study was approved by the Institute's Ethics Committee (IECPG-559/26–9-2019, RT-10/24–10-2019).

1.2. Risk grouping

Based on our institutional protocol, patients were defined as low risk if they had stage IA or IB with low grade and non-clear cell histology. These were advised close observation after surgery. Patients were defined as high risk if they had high grade tumor irrespective of stage subtype or those with stage IC, or stage II or clear cell histology. These patients were advised adjuvant chemotherapy with six cycles of pacli-taxel and carboplatin (AUC 5–6) every 3 weeks. Women age more than 70 years received single agent chemotherapy using carboplatin. Toxicity was recorded as per common terminology criteria for adverse events (CTCAE) 4.0 criteria.

1.3. Follow up

Patients were followed up every-three months during first two years, six monthly for next three years and yearly thereafter. On each visit patients underwent detailed physical examination, serum CA125 and ultrasound abdomen. Computed tomography (CT) scan abdomen/pelvis was done, if there was a rising serum CA125 or if patient became symptomatic.

1.4. Statistical analysis

Overall survival (OS) was calculated from the date of surgery to the date of death or last date of follow up. Relapse free survival (RFS) was calculated from the date of surgery to the date of relapse or last date of follow up. Survival probabilities were estimated according to the method of Kaplan-Meier and compared by the log rank test. Cox's regression model was used to analyse the significance of various factors affecting RFS and OS. Statistical analysis was carried out using STATA software version 13.0. Data has been censored on 31st December 2020.

2. Results

2.1. Baseline characteristics

During the study period, 1243 patients with ovarian cancer were registered, of which 1054 (84.7 %) were epithelial ovarian cancers (Fig. 1). Of these 195 (18.5 %) patients had early-stage EOC and were included in the current study. Baseline characteristics of the study population are given in Table 1 and Table 2. Stage I and II constituted 82 % and 18 % respectively. The median age at presentation was 47 years (range, 16 to 80 years). The most frequent symptom at diagnosis was abdominal pain (66 %) followed by abdominal distension (29 %) and vaginal bleeding (26 %). Serous histology (58 %), endometrioid (17 %) and mucinous (17 %) were common histologic subtypes. Patients with mucinous histology were a decade younger at the time of diagnosis (median age 34 years) as compared to other histologic subtypes. In 65 % of cases, high grade histology was noted, and 71 % of patients had elevated baseline serum CA125 values. The median CA125 values were higher (p = 0.03) in stage II (220 U/ml, interquartile range [IQR] 87–403) compared to stage IA/IB (73 U/ml, IQR 16–184) and stage IC (169 U/ml, IQR 22–535).

2.2. Treatment

The details of management in EOC in our study have been summa-rized in Table 3. One hundred eighty-four patients (94.0 %) underwent optimal staging surgery, while FSS was performed in 27 (14 %) patients. Lymph node dissection was not performed (inadequate surgical staging)
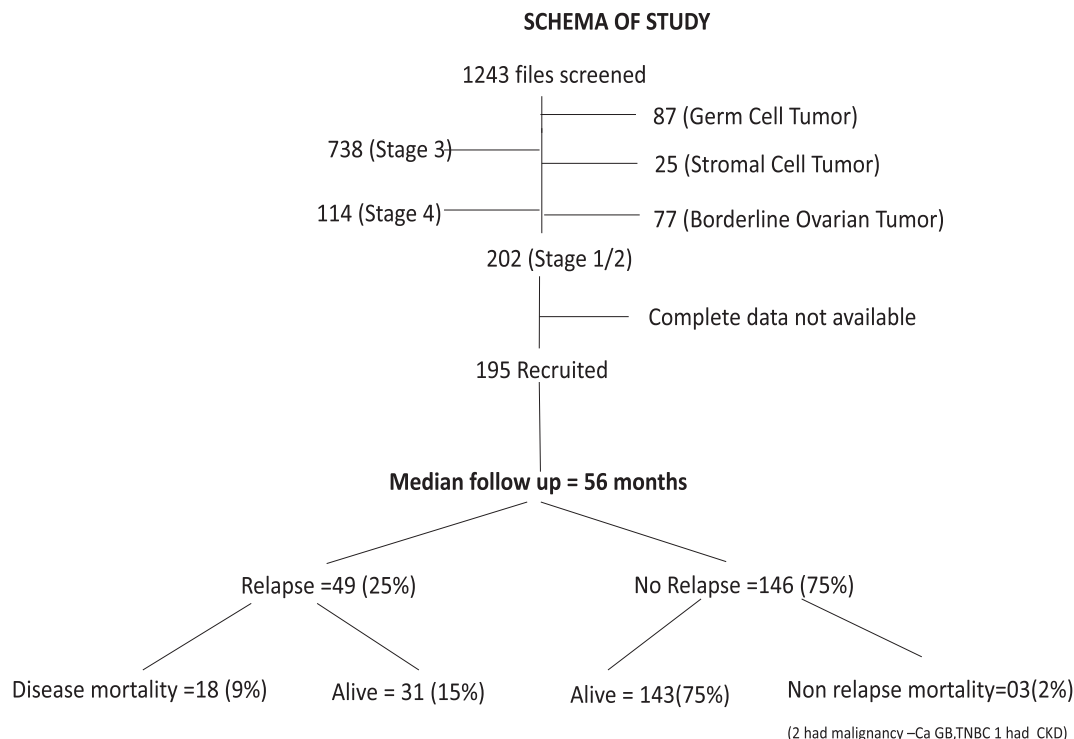
SCHEMA OF STUDY

Fig. 1. Study schema of the current study.

Table 1
Baseline characteristics of patients with Early Ovarian Cancer.

Baseline Characteristics	n = 195 (%)
Age (in years)	47 (16–80) years
Parity	
Nulliparous	41 (21.0 %)
Multiparous with 1 kid	25 (12.8 %)
Multiparous with greater than 1 kid	129 (66.1 %)
Symptom duration (years)	3 (0.1–18) months
Histology	
Serous	114 (58.4 %)
Endometrioid	33 (16.9 %)
Mucinous	33 (16.9 %)
Clear cell	13 (6.6 %)
Brenner's	01 (0.5 %)
Mixed type	01 (0.5 %)
Tumor grade	
High grade	117 (60.0 %)
Low grade	64 (32.8 %)
Not available	14 (7.1 %)
Baseline CA125	
< 35 U/ml	52 (26.6 %)
≥ 35 U/ml	130 (66.6 %)
Not available	13 (06.6 %)

Data is presented as mean (frequency). Age and symptom duration presented as median (range).

Table 2
Baseline staging according to FIGO 2014.

Baseline Stage	n = 1054 (%)
Stage I	**160 (15.1 %)**75
Stage IA	(7.1 %)17
Stage IB	(1.6 %)
Stage IC	21
Stage IC1	(1.9 %)30
Stage IC2	(2.8 %)17
Stage IC3	(1.6 %)
Stage II	**35 (3.3 %)**19
Stage IIA	(1.8 %)16
Stage IIB	(1.5 %)
Stage III	**738 (70.0 %)**
Stage IV	**114 (10.8 %)**
Data not available	07 (0.6 %)

FIGO Federation Internationale de Gynecologie et d Obstetrique.

(9.7 %). All grade neuropathy was seen in 38.3 % patients, while grade 3 or more neuropathy was only present in 3.7 % (n = 5) patients.

2.3. Relapse

At a median follow up of 56 months, 49 (25 %) patients had relapsed. All high-risk patients (n = 12) who did not receive adjuvant therapy, three (37.5 %) of eight patients who had residual pelvic deposits post-surgery and two (66.6 %) of three patients who underwent inadequate surgical staging eventually relapsed. Proportion of patient with baseline stage IA/IB, IC and II who relapsed were 18.4 % (n = 17), 27.5 % (n = 68) and 37.1 % (n = 35) respectively. Predominant sites of relapse (Table 4) were peritoneal (48.9 %), retroperitoneal lymph nodes (18.3 %), combined peritoneal and nodal (24.5 %), and distant relapse 4(8.1 %).

Out of the 49 patients who relapsed, 16 (32.6 %) patients underwent secondary cytoreduction followed by six cycles of chemotherapy (paclitaxel/carboplatin), and rest 33 (67.3 %) received only salvage

in three patients (1.5 %), while eight (4.1 %) patients had residual pelvic deposits after surgery. Median duration from date of surgery to start of adjuvant chemotherapy was 46 days (range, 32–62 days). Adjuvant chemotherapy was recommended for 145 patients (74.3 %) with high-risk disease, 133 patients (68 %) received adjuvant therapy, and 12 patients chose to remain under surveillance. Carboplatin and paclitaxel regimen was administered in 128 (96.2%) patients. Most patients (n = 127, 95.4 %) completed all their planned adjuvant chemotherapy cycles. Dose modification was required in only18 (14 %) patients. Most common ≥ grade 3 adverse effects observed during adjuvant chemotherapy were anemia (15.7 %), neutropenia (14.2 %) and thrombocytopenia

Table 3
Treatment characteristics of patients with Early Ovarian Cancer.

Treatment characteristics	n = 195 (%)
Type of Surgery	
Optimal Surgery	184 (94.3 %)
Residual disease after surgery*	08 (4.1 %)
Inadequate staging surgery**	03 (1.5 %)
Fertility sparing surgery***	27 (13.8 %)
Adjuvant therapy	
Yes	133 (68.2 %)
Observation	50 (25.6 %)
No#	12 (6.1 %)
Chemotherapy (n = 133)	
Paclitaxel Carboplatin	128 (96.2 %)
Single agent Carboplatin	03 (02.2 %)
Adriamycin Cyclophosphamide	01 (0.7 %)
Cisplatin Cyclophosphamide	01 (0.7 %)
Grade 3 or more toxicity (n = 133)	
Anemia	21 (15.7 %)
Neutropenia	19(14.2 %)
Thrombocytopenia	13(9.7 %)

Data is presented as mean (frequency).

*All patients had stage II disease with residual pelvic deposits.

** No lymph node dissection performed (two patients had stage I and one patient with stage II).

*** Unilateral salpingo-oopherectomy with complete surgical staging.

#Did not receive adjuvant therapy even though patients were high risk.

Table 4
Characteristics at relapse in patients with early EOC.

Characteristics of relapsed patients	n = 49 (%)
Time to relapse (months)	38 (3–96)
Time to relapse	
<12 months	08(16.3 %)
12–60 months	29(59.1 %)
More than 60 months	12(24.5 %)
Stage at baseline	
IA/IB (N = 92)	17(34.6 %)
IC (N = 68)	19(38.7 %)
II (N = 35)	13(26.5 %)
Sites of relapse	
Peritoneal	24(48.9 %)
Nodal	09(18.3 %)
Peritoneal + Nodal	12(24.5 %)
Distant*	04(08.1 %)

Data is presented as mean (frequency). Time to relapse presented as median (range).

EOC Epithelial ovarian cancer * Sites of distant relapse (liver, lung, and brain).

chemotherapy (Paclitaxel/Carboplatin or Liposomal doxorubicin/Carboplatin). Post salvage therapy complete or partial response was achieved in 42 (85.7 %) patients, while 04 (8.1 %) had stable disease and 03 (6.1 %) had progressive disease. Further lines of chemotherapy were administered in 25 (51.0 %) patients.

2.4. Fertility sparing surgery (FSS)

FSS consisted of unilateral salpingo-oophorectomy with preservation of the uterus and contralateral ovary, with staging procedures. Twenty-seven (13.8 %) patients [unmarried (n = 16), nulliparous (n = 8) or family not yet completed (n = 3)] opted for FSS. Median age was 25 years (range, 16 to 37 years). All patients had stage I disease [stage IA −16 (59.2 %), IC- 11 (40.7)], 23 (85.1 %) had low-grade tumors and 15 (56 %) patients had mucinous histology. Adjuvant chemotherapy was advised to 11 patients with stage IC, however, only eight patients received (three patients refused) adjuvant chemotherapy. All three patients who didn't opt for adjuvant chemotherapy relapsed at 6, 12 and 39 months. Two patients received salvage chemotherapy at relapse and

are alive in complete remission at last follow-up, while one patient who refused salvage chemotherapy died of progressive disease. Fertility outcomes were available for six patients, of which two patients successfully delivered five healthy babies.

2.5. Survival

Currently, 174 (89 %) patients were alive, 18 (9.2 %) patients had died of progressive disease while 03 (1.5 %) patients died of unrelated reasons- one each due to carcinoma gallbladder, triple negative breast cancer and chronic kidney disease. Kaplan-Meier probability of overall survival at 5 years is 87.6 % ± 3.1(95 % CI: 79.9–92.5) for all patients (Fig. 2). On univariate analysis as well as multivariate analysis only grade of the tumor was significant prognostic factor for OS (Table 5). Five-year relapse free survival (RFS) for all patients is 73.2 % ± 3.9 (95 % CI: 64.7–80.0); stage I −77 % and stage II −56 % (Fig. 2). RFS differences according to grade, histologic subtype (serous vs non-serous), stage and risk of relapse (low risk, high risk with chemotherapy and high risk without chemotherapy) has been illustrated in Fig. 3. Five-year RFS in low-risk patients on observation, high-risk patients who received chemotherapy and high-risk patients who didn't receive chemotherapy was 90.2 % (95 % CI: 71.6–96.9), 73.2 % (95 % CI: 62.7–81.2) and 25.0 % (95 % CI: 6.0–50.4) respectively. On univariate analysis (Table 5) stage, histologic grade, age, and type of surgery (optimal versus residual disease) were found to influence RFS. However, in multivariate analysis only grade of the tumor retained a prognostic role for RFS.

3. Discussion

In present study 195 patients with early-stage EOC were included, which constituted 18 % of all ovarian cancers. Median age at presentation was 47 years, which is younger compared to that of western cohort. According to SEER database, the median age of patients with ovarian cancer is 63 years. (Surveillance and Program, 2022). However, multiple retrospective studies have reported younger age (40–50 years) for early stage EOC at diagnosis, similar to present study. (Cannistra, 2004 Dec 9; Tropé and Kaern, 2007 Jul 10; Matz et al., 2017 Feb; Hsieh et al., 2019; Wei et al., 2016 Nov 11). Clinical presentation and median duration of symptoms prior to diagnosis is also alike (Cannistra, 2004 Dec 9; Tropé and Kaern, 2007 Jul 10; Matz et al., 2017 Feb; Hsieh et al., 2019; Wei et al., 2016 Nov 11). In present study 58 % patients had serous histology subtype and two third of all tumors were high-grade. There has been regional variation in the proportion of histologic subtypes with serous histology varying from 14 % in Japan (Hsieh et al., 2019) to 40 % in China (Wei et al., 2016 Nov 11). Other histologic subtypes endometrioid and mucinous were seen in 16.9 % each, while clear cell histology was reported in only 6.6 % patients in present study. In a Japanese study, clear cell histology was most common (37.5 %) followed by endometrioid (27.5 %), serous (14 %) and mucinous (13.3 %). (Wei et al., 2016 Nov 11). Although reasons for such geographic variation in histologic subtypes is unclear, population included in earlier studies was heterogeneous with higher proportion of advanced stage disease. Serum CA 125 was elevated in 71 % of patients in present study which is similar to report by Cuesta et al (de la Cuesta et al., 1999 Jun) but is higher than reported by Tognon et al. (Tognon et al., 2013) Relatively higher frequency of high-grade tumor and elevated CA 125 may be due to over representation of serous histology in present study. (de la Cuesta et al., 1999 Jun). Serum CA 125 values were minimally elevated in stage IA/IB, while values were comparatively higher in stage IC and stage II patients, suggesting a correlation with stage. Therefore, diagnosis of EOC at early stages (stage IA/IB) with higher serum CA 125 requires higher clinical suspicion for higher stage of the disease.

Fertility sparing surgery (FSS) was performed in about one fifth of patients with stage IA and IC disease. Most of these patients had low grade tumor and mucinous histology. Relapses were seen in 11 % of patients (all had high-risk features) who did not receive adjuvant
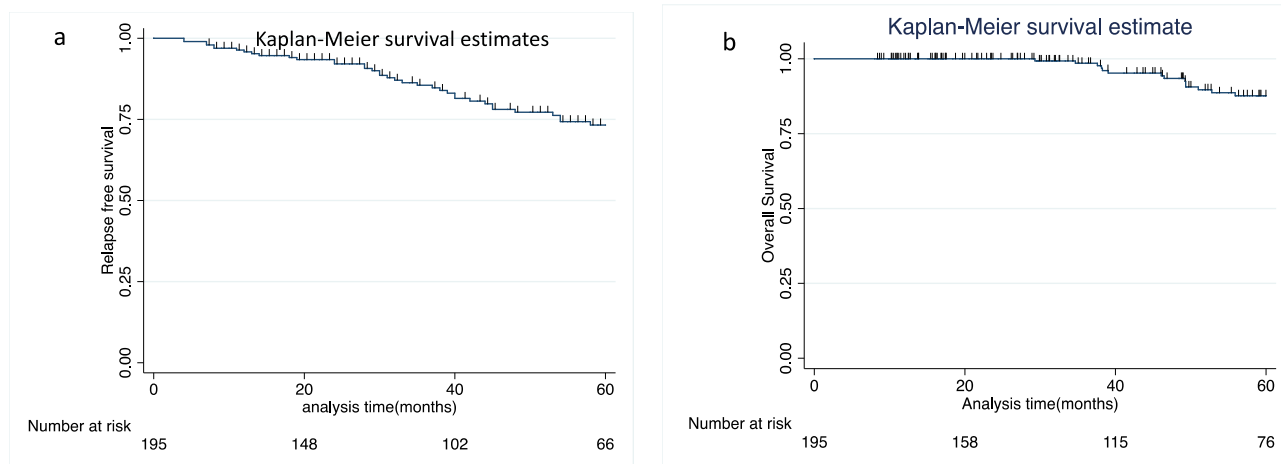
Fig. 2. Kaplan-Meier probability of a) relapse free Survival (RFS) and b) overall survival (OS).

Table 5
Predictive variables for relapse free survival (RFS) and overall survival (OS) in early EOC.

Parameters	Univariate analysis		Multivariate analysis	
	HR (CI)	p value	HR (CI)	p value
Relapse free survival				
Stage	2.0(1.1–3.9)	0.02	1.1 (0.5–2.4)	0.65
Grade	3.6(1.6–8.1)	0.002	2.9 (1.1–7.9)	**0.02**
Age	2.0 (1.1–3.7)	0.01	1.46 (0.7–2.7)	0.22
Histological subtype	1.1(1.0–3.3)	0.07	0.97 (0.4–2.0)	0.93
Surgery type*	2.4(0.9–6.1)	0.06	1.6 (0.5–4.7)	0.38
Overall survival				
Stage	2.0(0.7–5.2)	0.14	1.3(0.4–3.6)	0.57
Grade	11.0(1.4–82.8)	**0.01**	9.4(1.0–83.7)	**0.04**
Age	2.0(0.8–4.9)	0.10	1.4(0.5–3.6)	0.45
Histological subtype	1.1(0.7–5)	0.20	1.0(0.3–3.0)	0.99
Surgery type	0.8(0.1–6.1)	0.85	0.6(0.07–5.2)	0.67

EOC Epithelial ovarian cancer, HR hazard ratio, CI confidence interval, *surgery type (optimal versus sub-optimal) p value < 0.05 was considered significant.

chemotherapy. Similar results were reported by Kwon et al (4.7 %), Schlaerthet et al (15 %) and in a systemic review (15.7 %). (Schuurman et al., 2021 Feb 28; Liu et al., 2020 Apr 15; Kwon et al., 2009 Mar; Schlaerth et al., 2009 Oct) In a recent metanalysis including 2223 patients undergoing FSS, no difference in OS and RFS was observed between FSS and radical surgery. (Liu et al., 2020 Apr 15).

Patients with high-risk features were administered six cycles of adjuvant chemotherapy. Paclitaxel and carboplatin combination remains the preferred chemotherapy regimen for early-stage ovarian cancer. However, the optimal number of cycles of adjuvant chemotherapy remains debatable. (Young, 2003 Jan 15) In GOG157 trial, high-risk patients with early stage EOC were randomized to either three or six cycles of adjuvant chemotherapy (paclitaxel with carboplatin). Although no significant benefit was observed in overall population, patients with serous histology had improvement in survival with additional three cycles of chemotherapy. (Chan et al., 2010 Mar) In current study all high-risk patients who refused adjuvant chemotherapy relapsed, resulting in a worse five-year RFS for these patients than for those who received adjuvant chemotherapy. As most patients were salvaged at relapse, no difference in OS was observed. Due to high relapse rates in patients refusing adjuvant chemotherapy and fact that more than half of patients in our setting have serous histology, use of six cycles of adjuvant chemotherapy is warranted.

At a median follow up of 56 months, five-year RFS was 76.9 % and 55.9 %, while five-year OS was 89.4 % and 78 % for stage I and II, respectively. The results of this study confirm that the prognosis of early-

stage EOC is favorable which is consistent with previous studies. (Colombo et al., 2003; Trimbos et al., 2003; Trimbos et al., 2003 Jan 15; Swart, 2007) On univariate analysis, stage, grade, and age were found significant to influence relapse, however only grade of the tumor remained significant on multivariate analysis for both RFS and OS. This is consistent with earlier observations made by Hsieh et al. (2019) and Tognon et al. (2013)), while histologic grade was not a significant predictor for survival in the study by Wei et al. (2016 Nov 11) Most studies (Supplementary Table 1) have reported stage to be significant prognostic factor for RFS as well OS. However, in present study tumor stage lost significance on multivariate analysis. This could be due to a small absolute number of patients. Unlike in study by Hsieh et al. (2019), histology and elevated CA 125 levels were not significant prognostic markers in our study.

Present study includes large data for early-stage EOC in Indian patients with outcome comparable to international studies despite higher frequency of high-risk features. Current study also presented real world evidence of efficacy of six cycles of adjuvant chemotherapy in high-risk early-stage EOC. This will provide greater confidence for use of six cycles especially in high grade and serous histology. Feasibility of FSS in selected patient is further reinforced.

Due to limitation of retrospective design and missing toxicity data, treatment related adverse effects may have been under-reported in the study.

Conclusion: Early-stage ovarian cancer constitutes about one fifth of all cases with EOC. Patients present at a younger age and have predominant serous histology with high grade tumors. Long term outcomes are excellent. However, patients with FIGO Stage II and high-grade tumor are at higher risk of relapse and need adjuvant therapy and closer follow up. Histologic grade is an important prognostic factor for relapse and survival. Fertility sparing surgery may be considered in selected stage I patients without impacting survival.
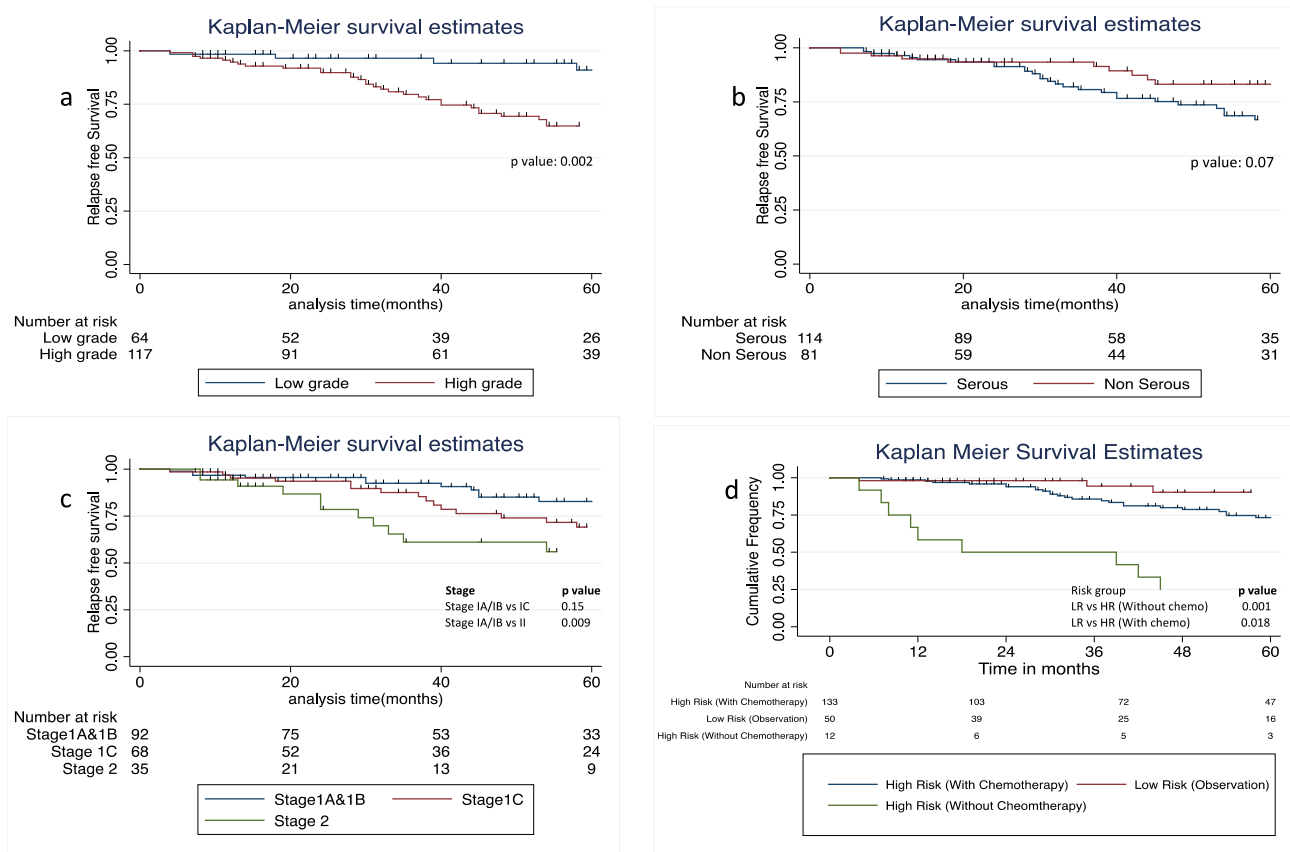
Fig. 3. Kaplan-Meier probability of relapse free Survival (RFS) according to a) Grade b) Histologic subtype (serous vs non-serous) c) Stage and d) Risk group.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2022.101083.

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