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INFLUENCE TO CHOOSE TREATMENT METHODS ON PROGNOSIS OF RECURRENT OVARIAN CARCINOMA

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ABSTRACT

Objective: The main purpose of this study was to evaluate the prognosis of patients with recurrent epithelial ovarian cancer in the Tianjin Obstetrics and Gynecology Hospital in Tianjin; to evaluate the difference in the efficacy of secondary cytoreductive surgery or chemotherapy alone in patients with recurrent epithelial ovarian cancer; The difference in quality of life between the two treatment regimens after treatment. **Methods:** The hospital records for patient with ovarian carcinoma of Tianjin Central hospital of Obstetrics and Gynecology was reviewed prospectively from February 2017 to March 2019 which included patients age, presenting complaint, associated symptoms if any, duration of disease, clinical features, menstrual history, details of physical examination, results of imaging studies if any, results of office biopsy if performed, operative procedure, and pathology diagnosis from the surgical specimen. The serum levels of CA125(IU/ml), HE4(Pmol/ml) were investigated from initial presentation of disease and during the treatment course and have also been recorded and reported. Two groups are formed for comparison, group A is recurrent cases who received surgery and group B recurrent cases receiving chemotherapy alone. There are 20 patients in group A and 17 patients of group B. The diagnosis of epithelial ovarian carcinoma was entirely based on the histopathology and immunohistochemistry. All the data were analyzed by SPSS 22.0 statistical software. A comparative analysis of two groups compared using chi square test was done. The difference of $P < 0.05$ was statistically significant. **Results:** A prospective observational study was performed on 40 patients with recurrent epithelial ovarian cancer who were admitted to the Tianjin Obstetrics and Gynecology Hospital from February 2017 to March 2019. Of the 40 patients, 11 were stage I of epithelial ovarian cancer, 4 were stage II of epithelial ovarian cancer, 22 were stage III of epithelial ovarian cancer, and 1 case was stage IV of epithelial ovarian cancer. Among them, 12 patients were younger than or equal to 50 years old, and 25 patients were older than 50 years old. In the initial treatment, 35 patients underwent initial cytoreductive surgery, and 2 patients underwent neoadjuvant chemotherapy; 24 patients underwent lymph node resection in the initial treatment and 13 patients did not have lymph node resection. In the 37 patients with recurrent epithelial ovarian cancer, in the second treatment, considering the patient's wishes, the current state of the body and the progress of the disease, 20 patients underwent secondary cytoreductive surgery, and 17 patients underwent chemotherapy alone. Univariate analysis of complete remission rate was associated with treatment (secondary cytoreductive surgery or chemotherapy alone), P = 0.011, OR = 8. Related to the CT value, P=0.018. With the first surgical procedure (initial cytoreductive surgery or neoadjuvant chemotherapy), age (≤50 years or older), whether lymph nodes were removed during initial treatment, patients were in stage of epithelial ovarian cancer (I II III IV Period), CA125 and HE4 values are irrelevant. Multivariate analysis of CT values and OR values of treatment methods, CT = OR = 2.431 (95% CI 1.12 - 5.289), (P = 0.025); OR of treatment mode was 8.391, and the lower limit of 95% confidence interval was 1.194. The upper limit of the 95% confidence interval is 58.969 (P = 0.03). In the 20 patients with secondary cytoreductive surgery, the median disease-free progression (PFS) was 30 (95% CI 21.5-38.5) months, and the simple chemotherapy-free 17 patients had a median disease-free progression (PFS) of 11 patients. (95% CI 8.4-13.6). **Conclusion:** In this study, we obtained statistically significant differences in the efficacy of secondary cytoreductive surgery or chemotherapy alone in patients with recurrent epithelial ovarian cancer. In order to improve the quality of life of patients with recurrent epithelial ovarian cancer, the physical condition of the patient,It is advisable to take secondary cytoreductive surgery for patients with recurrent epithelial ovarian cancer. In some patients with epithelial ovarian cancer after primary surgery and a platinum-sensitive recurrent tumor, complete resection of the recurrent tumor during secondary cytoreductive surgery improves progression-free survival and overall survival. Our results suggest that a long treatment-free interval and non-disseminated lesions (three or fewer lesions) on radiographic images could be useful predictors of complete resection during secondary cytoreductive surgery.

KEYWORDS: Secondary cytoreductive surgery epithelial ovarian cancer no visible residuals progression-free survival and treatment-free interval platinumsensitive.

INTRODUCTION

1. Background

Ovarian cancer is a disease that initially spreads throughout the abdominal cavity, although in some cases a pleural effusion or extraperitoneal spread can be detected. The mortality associated with ovarian cancer is primarily due to dissemination of the disease within the peritoneal cavity due to the absence of early diagnostic symptoms. When the peritoneal cavity is involved, conventional therapies such as surgery and chemotherapy in most of the cases fail to provide long-term cure. It is a biologically aggressive cancer with exceptionally high mortality rate, making it the fifth most common causes of death from malignancy in women.[1] Up to 80% of these women experience a relapse that can eventually lead to disease progression and death. Most women with ovarian cancer are in the fifth or sixth decade of their lives. The lifetime risk of ovarian cancer is 1.4% (1 in 70). The majority of patients with ovarian cancer have advanced disease at the time of initial diagnosis, which is closely related to the poor prognosis of the disease. Minimal changes in mortality over the last 40 years.

Worldwide, ithere iare imore ithan i200,000 icases iof iovarian icancer ieach iyear, iaccounting ifor iabout i4% iof iall icancers idiagnosed iin iwomen. iThe irisk iof iovarian icancer iin iwomen iunder ithe iage iof i75 ivaries ifrom icountry ito icountry ibetween i0.5% iand i1.6%, iwhich icorresponds ito ia istandardized iovarian icancer irate. iThe iage ivaries ibetween i5 iand i14 icases iper iyear iper i100,000 iwomen iunder i75 iyears[2]. iIn iEurope, i37 ito i41% iof iwomen iwith iovarian icancer ilive ifive iyears iafter idiagnosis. iThe ilow isurvival irate iassociated iwith iovarian icancer iis ilargely idue ito ithe ifact ithat imost iwomen iare idiagnosed iwhile ithe icancer iis ialready iadvanced. iEpithelial iovarian icancer iis ia idisease icharacterized iby ithe iformation iof imalignant icells iin ithe itissue iof ithe iovary[3]. iIt iaccounts ifor iapproximately i90% iof iovarian icancers, iwith ithe iremaining i10% iderived ifrom igerm icells, isex icord iand istroma iof iovary. iAbout i75-80% iof iepithelial iovarian icancers iare ihistologically iserous, iless icommon iare imucinous i(10%), iendometrioids, iclear icells, iBrenner iand iundifferentiated icancers i(Scully, i1998). iMost iwomen iwith iovarian icancer ihave iextensive idisease iat ithe itime iof ipresentation i(FIGO istage iIII-IV)[2]. i

This imay ibe idue ito ithe irelatively iearly ispread iand iimplantation iof ihigh-grade iserous icancers iin ithe iremaining iperitoneal icavity. In iaddition, isymptoms isuch ias iabdominal ipain iand iswelling, igastrointestinal isymptoms iand ipelvic ipain iare ioften inot irecognized, iwhich imay idelay ithe idiagnosis i(Goff i2000, iSmith i2005).

Survival irates idepend ion imany ifactors iincluding itumor istage iand ipatient iage iat idiagnosis2,3; iin ipatients iwith iearly istage idisease, i5-year isurvival iis i80% ito i90%, iwhile iit iis iapproximately i25% ifor ithose iwith iadvanced istage idisease, iwhich iis idiagnosed iin iapproximately itwo ithirds iof icases.4 iThe iprimary iintervention ifor iadvanced istage iovarian icancer iis idebulking isurgery ifollowed iby ichemotherapy iwith iplatinum-based ianalogues iand ipaclitaxel iand/or ineoadjuvant ichemotherapy ifollowed iby idebulking isurgery iand iadjuvant ichemotherapy. iDespite ithe iimproved imedian ioverall isurvival iin ipatients iwith isuch ichemotherapy iregimens, irelapse istill ioccurs iin ithe imajority iof ithose iwith iadvanced idisease, iand ionly i10–30 i% iof isuch ipatients ihave ilong-term isurvival, imost ipatients iwill ipresent iwith irecurrent idisease iwithin i12 ito i18 imonths.4 iSurvival irates iare iworse iin iplatinum-refractory idisease, inot iexceeding i5 imonths.5

Although ithe ithree iprimary igynecological imalignancies ihave ihistorically ibeen iconsidered ito ibe idistinct idisorders, iit iis icurrently iknown ithat iovarian iepithelial, itubal iand iperitoneal icarcinomas iare ipart iof ia ifamily iof igynecological iadenocarcinomas iderived ifrom ithe iMullerian icompartment i[4].Epithelial icarcinomas iof ithe iovaries, itubes, iand iperitoneum iare icollectively ireferred ito ias iovarian iepithelial icancers i(OCCs). iBased ion idata ireported ifor ithe iperiod i2012-2014, iit iis iestimated ithat iabout i1.3% iof iwomen iin ithe iUnited iStates iwill ibe idiagnosed ias iEOC iat isome ipoint iin itheir ilives i[4]. iThe iapproximate inumber iof inew icases idiagnosed iin ithe iUnited iStates iin i2017 iwas iestimated iat iover i22,000, iand imore ithan i14,000 ideaths ioccurred iin ithe isame iyear. iThe irelative isurvival ifor ilocalized iEOS iafter ifive iyears iis iover i90% i[4]. iUnfortunately, idistant imetastases iwith ia irelative isurvival iof ionly i30% ifor ifive iyears iare imore ilikely ito ihave iEOC idiagnosed iat ia ilater istage. iDespite iaggressive isurgical itreatment iand ichemotherapy, ithe imajority iof ithese iwomen ieventually isuffer ifrom itheir idisease[5, i6]. iAs itraditional ichemotherapy imay ihave ireached iits ilimit, iattention ihas ishifted ito inew itherapies, ialternative idosing iand imaintenance itherapy. iThe irecent iimprovements iin idisease icontrol iby imaintenance itherapy irepresent ia isignificant iadvancement iin ithe itreatment iof iselected ipatients[7]. I

The istandard itreatment ifor iepithelial iovarian icancer i(EOC) iusually iconsists iof ia iprimary ioperation ifor icomplete icytoreduction, ifollowed iby isix icycles iof icarboplatin iand itaxanes ievery ithree iweeks[8]. iIn icomorbid icases, ichemotherapeutics iare ioften imodified ito iavoid ipotential iside ieffects. iIn isome ipatients iwith ipoor iperformance iand i/ ior iadvanced idisease, ichemotherapy i(neoadjuvant) iis iperformed iprior ito isurgery[9]. iComplete icytoreduction iafter iprimary isurgery iand ithe iduration iof ithe inon-treatment iinterval iafter iprimary ichemotherapy iare iindependent iprognostic ifactors ifor ithe isurvival iof iEOC ipatients[10].

Epithelial iovarian icancer irecurs iin iup ito i75% iof ipatients, ieven iin ipatients iundergoing icomplete icytoreduction iafter iprimary isurgery i[8]. iOnce ithe iinitial itreatment iis icompleted, ipatients iare imonitored ifor irecurrence iand imust ibe itreated ifurther. iTumors iare iconsidered ito ibe isensitive ito iplatinum iif irecurrence ioccurs iat ileast isix imonths iafter icompleting iprimary ichemotherapy. iThese ipatients iusually ireceive iplatinum-based ichemotherapy i(PBC) ias ia isecondary itreatment[11]. iIn irecent idecades, ihowever, iimproved isurvival ihas ibeen iobserved iin ipatients iwith irecurrent iEOC iwho iundergo isecondary icytoreductive isurgery i(SCS), iin iwhich ithe ivisible itumor iis icompletely ieliminated, ifollowed iby iPBC, icompared ito ithose ireceiving iCBP ialone.

A iGerman iworking igroup, ithe iArbeitsgemeinschaft iGynakologische iOnkologie i(AGO), ihas iattempted ito istructure ithe irecommendations ifor ithe iSCS i(AGO iscore) iin ithe istudies iDESKTOP iI[12] iand iII itrials[13]. iDESKTOP iIII i(10) iis ian iinternational, imulticentre, irandomized, icontrolled itrial i(RCT) ithat iprospectively iassesses iwhether iSCS ifollowed iby iPBC iimproves isurvival iin ipatients iwith irecurrent iEOC iand ia ipositive iAGO iscore[13] icompared ito iimproved ipatients itreated iwith ithis idrugs icompared iwith ithose iwho ireceive iPBC ialone. iPatients ienrolled iin iDESKTOP iIII ihad ito iundergo icomplete icytoreduction ifollowing iprimary isurgery, iwith ithe ifirst irelapse ioccurring iat ileast isix imonths iafter icessation iof itreatment iof iprimary iPBC iand iless ithan i500 iml iof irecurrent iascites. iThe ientries ifor iDESKTOP iIII iare inow icomplete iand ithe iresults iare iexpected ishortly. I

The iNorwegian iguidelines irecommend icriteria isimilar ito iAGO ifor ithe iselection iof ipatients iin iSCS iand iPBC ior iPBC i(since i2007). iHowever, iSCS ican ibe ioffered ito ipeople iwith ilocalized idisease ipreferences iindependent iof iTFI iand ieven ipatients iwith iTFI iolder ithan i24 imonths iwith idisseminated idisease[14]. I

Quality iof ilife iis ian iimportant ioutcome ifor ithe ipatient. iHowever, ithere iare ifew idata ion iquality iof ilife iin iovarian icancer ipatients iand itheir ieffects ion itreatment, iespecially iin iwomen iwith irecurrent idisease. iIt iis inot isurprising ithat ia idiagnosis iof iovarian icancer iis iassociated iwith iincreased istress iand ireduced iquality iof ilife. iMore ithan ihalf iof iwomen ibelieve ithat isuch ia idiagnosis iwould ichange itheir icourse iof ilife, iwhile imost ialso istated ithat isurgical iscars, iweight igain iand ihair iloss iare ione iof itheir imain iconcerns. iPatients iin ineed ialso ihave ia imuch iworse ifunction, imore iproblems iand ia ilower iquality iof ilife ithan ipatients iwithout istress. iPrevious istudies ihave ishown ithat iit imay ibe iimportant ifor ipatients ito imaintain ihope ifor ihealing, iothers ihave iquestioned ithe ivalue iof igiving ihope ito ipatients, ias ifalse ihopes ican iincrease ithe irisk iof idepression iand iother iill ieffects ion iwell-being. iThis isuggests ithat iinterventions iand iadditional istrategies iare ineeded ito icommunicate iand isupport iwomen iwith iovarian icancer. iPatients iundergoing ipalliative ichemotherapy ihave ibeen isuggested ito ibe iunrealistic iin itheir iexpectations, ieven iwhen iassociated iwith iemotional ibenefits, iOverall ifunction iand iquality iof ilife. iIn igeneral, iwomen iwith irecurrent iovarian icancer iseem ito ihave ihigh itreatment iexpectations idespite icomplex isymptoms iand isignificant isymptom iburden. iIn iaddition, iit ihas ialso ibeen ireported ithat ithere iare ino isignificant idifferences iin ithe iseverity iof ithe istress iand iself-reported iproblems iin ipatients iwith iand iwithout irecurrence. iThe iburden, iif ipresent, ileads ito iproblems iof iphysical iand iemotional ifunctioning iof ithe ipatients iwith ione ilower iquality iof ilife. iDue ito ithe ilack iof iavailable iQoL idata iin iwomen iwith iovarian icancer, iespecially iin ipatients iwith irecurrent idisease, iand ito iinvestigate ithe ipotential iimpact iof irecurrence ion iquality iof ilife, iwe iconducted isurvey ito iinvestigate ithe iperspectives iof ithe ipatient irelative ito idaily ilife iand ioutlook ifor ithe ifuture.

2. METHODS AND MATERIALS

2.1 Study population

The target population was the EOC patients who were cured at Tianjin central hospital of gynecology and obstetrics from February 2017 to March 2019. The patients were operated by surgical staging. After that, the patients were treated by chemotherapy by paclitaxel and carboplatin formula every three weeks for six cycles. After taking completed treatment, then took monitoring of CT, HE4 and CA125 results for one month. Then it was monitored every three months until the end of the research.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria: 20 to 70 years old Patients were enrolled. Every case of patients who were proved that being an epithelial ovarian cancer FIGO stage III-IV. They had been complete treatment by surgery and adjuvant chemotherapy six cycles from February 2017 to March 2019. Complete cytoreduction at the primary surgery, no ascites at the time of recurrence (<500 mL). These patients were treated in our hospital for the first recurrence. Patients who had a clinical, radiographic, and serologic, platinum-free interval (PFI) for 6 months after the primary surgery and platinum-based first-line chemotherapy were considered for inclusion. Also, they must make consent to participate in the study.

Exclusion criteria: We excluded patients with no gross disease identified by imaging techniques. Patients who visited our hospital for second-look operations or palliative surgery were also excluded. Patients with non-EOC, synchronous cancer or other cancers prior to EOC diagnosis were excluded from the study. The patients

who had been diagnosed that being an epithelial ovarian cancer but refused to participate in the study.

2.3 Monitoring and Data collection

This prospective cohort study was approved by the ethical committee of Tianjin central hospital of gynecology and obstetrics. The inclusion population were those common EOC FIGO stage III-IV who were diagnosed and treated at Tianjin central hospital of gynecology and obstetrics during February 2017 to March 2019. Those who refused were excluded from the study. The diagnosis were done by gynecologic oncologists with physical examination, abdominal ultrasonography, chest and abdominal X-rays and CT scan or MRI in some selected patients. Surgical exploratory laparotomy with cytoreductive surgery were done with complete or incomplete resection.

The patients were followed up every month after completion of chemotherapy courses with routine physical examination, chest or abdominal X-rays, CT scan, MRI or chest, abdomen or pelvic cavity. In biomarker with CA- 125 and HE4 levels less than doubled from post-operative biomarker defined as “non-rising” while those who had CA-125 and HE4 increase two folds from post-operative biomarker were defined as “rising”.

The following data were collected from the medical records which included patients age, presenting complaint, associated symptoms if any, duration of disease, clinical features, menstrual history, details of physical examination, results of imaging studies if any, results of office biopsy if performed, operative procedure, and pathology diagnosis from the surgical specimen. The serum levels of CA125(IU/ml), HE4(Pmol/ml) were investigated from initial presentation of disease and during the treatment course and have also been recorded and reported. Two groups are formed for comparison, group A is recurrent cases who received surgery and group B recurrent cases receiving chemotherapy alone. There are 20 patients in group A and are designated in numbers from 1-20 and the 17 patients of group B are also designated in numbers from 1-17. The diagnosis of epithelial ovarian carcinoma was entirely based on the histopathology and immunohistochemistry.

3. RESULTS

3.1 Patient characteristics

Of the 40 patients included in this study, 23 were treated with SCS plus chemotherapy (SCS group) and 17 were treated with chemotherapy alone (CT group). In the entire cohort, the distributions of age, International Federation of Gynecology and Obstetrics (FIGO) stage, histo-logical type, primary therapy, and recurrence site were not significantly different between the 2 groups).

The proportion of patients in the SCS+PBC group was evenly distributed throughout the enrollment years (data not shown). 3 patients from overall treatment group was lost to follow-up. There was no difference in the distribution of FIGO stages between the SCS+PBC and the PBC group. The majority of patients represented FIGO stages III (Table 1).

Of the 40 patients, 11 were stage I of epithelial ovarian cancer, 4 were stage II of epithelial ovarian cancer, 22 were stage III of epithelial ovarian cancer, and 1 case was stage IV of epithelial ovarian cancer. Among them, 12 patients were younger than or equal to 50 years old, and 25 patients were older than 50 years old. In the initial treatment, 35 patients underwent initial cytoreductive surgery, and 2 patients underwent neoadjuvant chemotherapy; 24 patients underwent lymph node resection in the initial treatment and 13 patients did not have lymph node resection. In the 37 patients with recurrent epithelial ovarian cancer, in the second treatment, considering the patient's wishes, the current state of the body and the progress of the disease, 20 patients underwent secondary cytoreductive surgery, and 17 patients underwent chemotherapy alone. Univariate analysis of complete remission rate was associated with treatment (secondary cytoreductive surgery or chemotherapy alone), P = 0.011, OR = 8. Related to the CT value, P=0.018. With the first surgical procedure (initial cytoreductive surgery or neoadjuvant chemotherapy), age (≤50 years or older), whether lymph nodes were removed during initial treatment, patients were in stage of epithelial ovarian cancer (I II III IV Period), CA125 and HE4 values are irrelevant. Multivariate analysis of CT values and OR values of treatment methods, CT = OR = 2.431 (95% CI 1.12 - 5.289), (P = 0.025); OR of treatment mode was 8.391, and the lower limit of 95% confidence interval was 1.194. The upper limit of the 95% confidence interval is 58.969 (P = 0.03). In the 20 patients with secondary cytoreductive surgery, the median disease-free progression (PFS) was 30 (95% CI 21.5-38.5) months, and the simple chemotherapy-free 17 patients had a median disease-free progression (PFS) of 11 patients. (95% CI 8.4-13.6).

There were 16 EOC patients with serous histology in the SCS+PBC group, compared with 14 in the PBC group (Table 1). Correspond-ing numbers for endometroid, mucinous, clear-cell and non-classified adenocarcinomas are shown in Table 1. There were no differences in comorbidity between the two treatment groups (data not shown).

Age groups at first recurrence were equally represented in the two treatment groups (p = 0.847, Table 2). Computed tomography (CT) was the pre-dominantly used imaging method at recurrence.However, the cancer antigen 125 (CA125) level at PR was significantly higher (239.3 ±194.7 vs 128.3 ±148.6, P =.081), HE4 was significantly shorter (100.9 ±58.6 vs 358.8 ± 145.9, P =.591), and CT group was significantly lower (P =.018) in the PR group than in the CR group. There were no significant differences in the baseline characteristics

between the 2 groups for the tumour markers CA125 and HE4, whereas CT is significant in the entire cohort (Table 3).

3.2 Survival analysis in the entire cohort

In the entire cohort, the mean follow-up for survivors after chemo is lower than surgery. The median survival time after surgery is more than chemo. 3 patients was lost to follow-up. Of the 40 total patients, all patients relapsed and 8 patients died. Among the entire cohort, the overall survival (OS) rates were between 21.5 to 38.4.

On comparing the treatment outcomes between the 2 treatment groups, OS was significantly longer in the SCS group than in the CT group (Fig. 1). These findings indicate that SCS improves OS.

The results of another multicenter RCT, GOG 213 trial, will also be published shortly. The SOCceR study had recruiting problems and was terminated prematurely. In a retrospective and population-based Dutch study, these patients had a complete secondary cytoreduction of 72% and a mean survival of 51 months.[79]

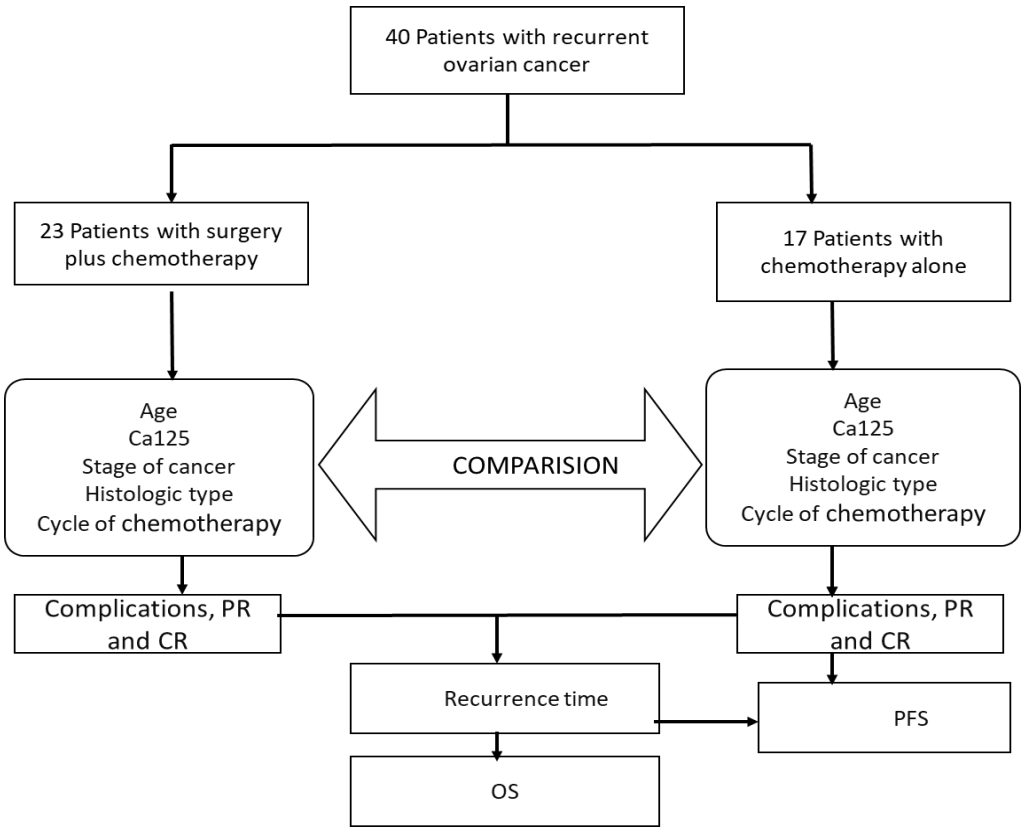

Figure 1: Flow chart illustrating the data sources and inclusion criteria for epithelial ovarian cancer (EOC) patients diagnosed from february 2017 to march 2019. The study subjects included in the two treatment groups (n = 40): platinum-based chemotherapy (PBC) alone and secondary cytoreductive surgery(SCS+PBC); hospital-based data.

Table 1: Clinical and Histopathologic Characteristics of the 40 Patients with Epithelial Ovarian Cancer.

Prognostic indicators	Total Number of Patient	chemotherapy	Surgery	p-value
Age				
≤ 50	15*	6	9	0.847
> 50	25	11	14	
FIGO Stage				
I	11	4	7	0.936
II	4	1	3	
III	22	11	11	
IV	1	1	0	
Histologic Type				
Serous	30	14	16	-
Mucinous	0	0	0	
Endometrioid	3	0	3	
Other	7	3	4	

* 3 patients from overall treatment group was lost to follow-up.

Single factor analysis

Table 2: Single factor analysis.

Therapy	surgery	20	P=0.011	OR=8
	chemo	17		
First operation	PDS	35	P=0.473	
	NACT	2		
Age	≤50	12	P=0.847	
	>50	25		
lymphadenctomy	Yes	24	P=0.241	
	No	13		

Table 2.2: This table includes single factor analysis. It compares between complete regression and Partial regression, test done is chi square test. This table signifies that complete regression is possible with therapy where time of first operation, age of the patient and lymphadenectomy are not significant.

Table 3: The stage of the carcinoma.

		n	
Stage	I	11	P=0.936
	II	4	
	III	22	
	IV	1	

This table includes the stage of the carcinoma. We can see that majority of the patient presented at FIGO stage III followed by stage I and least was Stage IV. The table clearly depict p value is more than 0.05, so it can be concluded that stage of the carcinoma has no significant impact on the presentation of the patient in our study.

Table 4: The investigation done for the epithelial ovarian carcinoma.

	CR	PR	
CA125	128.3±148.6	239.3±194.7	P=0.081
HE4	358.8±145.9	100.9±58.6	P=0.591
CT	6	4.5	P=0.018

This table include the investigation done for the epithelial ovarian carcinoma in the patient included in this study, for comparision t test was done. It shows that tumor marker like CA125 and HE4 are not significant, whereas CT is significant. So it can be concluded that CT is superior to other two test and if CT was available for all the patient complete regression would have been possible in more cases.

Table 5: CR/PR.

		B	Sig.	OR	95% C.I.for OR	
					Lower	Upper
Step 1[a]	CT	.888	.025	2.431	1.118	5.289
	therapy	2.127	.033	8.391	1.194	58.969
	Constant	-4.724	.034	.009		

Variable(s) entered on step 1: CT, therapy1surgery0chemo.

This Table shows multifactorial analysis between complete and partial regression. It shows that CT and therapy are two independent factor. They individually affect the outcome but are independent of each other.

Table 6: Means and Medians for Survival Time

Therapy (1surgery 2chemo)	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
1	35.430	5.616	24.422	46.438	30.000	4.325	21.524	38.476
2	13.438	1.814	9.883	16.992	11.000	1.333	8.387	13.613
Overall	27.011	3.960	19.250	34.772	24.000	2.483	19.133	28.867

Estimation is limited to the largest survival time if it is censored.

This table is of means and median for the survival time. Mean survival time after surgery is between 24.2 to 46.4 months whereas for chemo is 9.8 to 16.9 which is clearly lower than surgery and overall survival is between 19.2 to 34.7.

The median survival time after surgery is between 21.5 to 38.4 which is more than chemotherapy and overall median survival is between 19.1 to 28.8.

Table 7: Overall Comparisons.

	Chi-Square	Df	Sig.
Log Rank (Mantel-Cox)	10.632	1	.001

Test of equality of survival distributions for the different levels of therapy(1surgery 2chemo).

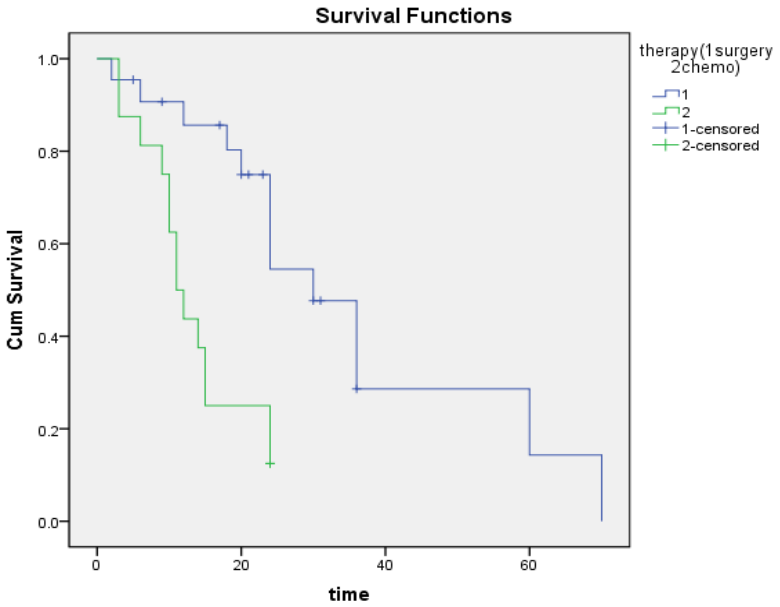

Figure 2: Survival from first recurrence in the cohort of 40 epithelial ovarian cancer patients diagnosed in 2017–2018 in Tianjin central hospital of gynecology and obstetrics with complete cytoreduction after primary surgery and platinum-sensitive tumors at first recurrence: 23 treated with secondary cytoreductive surgery and platinum-based chemotherapy (SCS+PBC) and 17 treated with PBC alone; population-based data. This graph clearly depicts that survival time post-surgery is more than after chemotherapy.

4. DISCUSSION

Our prospective, hospital-based study demonstrated that EOC patients (all FIGO stages) with good performance status and with complete cytoreduction after primary surgery followed by PBC and first recurrence more than six months after completion of primary treatment, had improved OS when treated with SCS resulting in complete resection compared with either PBC alone or SCS with some visible residuals. This is in agreement with previous studies.[80, 81]

The strength of the study is the long follow-up time, detailed, high-quality data on first and second recurrence, and continuous surveillance of patients without exclu-sions due to advanced age or loss to follow up. Indeed, loss to follow up can be an obstacle in international RCTs; the DESKTOP III trial had an estimated 10% loss to follow up. Recruitment to international RCTs may be influenced by differences in healthcare systems between countries, private insurance coverage, and socioeconomic status, which could lead to selection bias. Patients treated with SCS who refuse to give informed consent to partici-pate in a RCT could also introduce bias. Some RCTs are difficult to conduct.

To compare survival in two treatment groups. Follow-up data are systematically gathered and evaluated without recruitment problems or exclusions due to age or poor health conditions. All age groups are represented in our hospital-base study. This type of clinical research is considered to be of high quality and to gener-ate satisfactory evidence for clinical practice,but espe-cially for fields in which RCTs are difficult to conduct. With its complete, high-quality, population-based cancer registry, China is an ideal country for a PACE study. Moreover, as there is little difference in treatment among EOC patients due to the national healthcare sys-tem in China, and patients are followed throughout their lifetime at this hospital, the PACE approach may contribute to the

validation of SCS and PBC vs. PBC alone when compared with results from other studies.

Our study is prospective, with known limitations, and is not free from selection bias. In Tianjin, patients with first recurrence are usually referred to the gynecologic oncology department of a teaching hospital, where a mul-tidisciplinary tumor board considers whether they should undergo SCS and PBC or PBC alone. Patients are selected to SCS and PBC based on a long TFI, the platinum sensi-tivity status, the presence of non-disseminated lesions in radiological images, lack of ascites, and good performance status.[14] These clinical criteria differ from those of the DESKTOP III study with a positive AGO score.[13] Our study indicates that such selection led to a resection rate at SCS comparable to the results of others.[79] It seems that the treatment with SCS, providing complete cytoreduction, has a beneficial effect on OS compared with either the patients with residuals after SCS or those treated with PBC alone. Additionally, our finding of five-year survival rate among patients from the SCS group whose radiological lesions were disseminated, may be interpreted as a positive result of SCS with complete resection. We identified patients in both groups for whom planned PBC was changed. The proportion of these patients did not differ between treatment groups and did not influence survival analyses substantially. We observed longer TFIs and a smaller proportion of dissem-inated radiological lesions in the SCS+PBC compared with the PBC group. TFI and well-defined, non-dissemi-nated lesions seemed to predict longer PFS. The small number of identified confounders, presented in a simple, dichotomized way, is a weakness of this study.

Non-disseminated lesions in radiological images may reflect the resectability of a recurring tumor. Our observation of a higher proportion of non-disseminated lesions at first recurrence in the radiological images of the SCS+PBC group compared with PBC group, is in accordance with previous findings.[81,82] However, patients with disseminated lesions at first recurrence were also present in the SCS+PBC group and showed improved five-year survival rate after complete resection. Conversely, we cannot explain why some patients from the PBC group with non-disseminated radiological lesions and long TFI were not treated with SCS. It is probable that lesions at difficult locations introduced high complication risks and the gynecologic oncologist did not recommend SCS+PBC. Unfortunately, in the hospital records obtained for many patients in our study, details were missing on the dissemination in the descriptions of radiological images at first recurrence. There were more patients is in the SCS+PBC group than in the PBC group. The proportion of patients that received tertiary PBC after second recurrence was similar in both treatment groups, but there were more patients without second recurrence and alive at the end of follow up in the SCS+PBC group. Investi-gation of platinum sensitivity beyond second recurrence in the SCS+PBC and PBC groups should be evaluated in future studies.

We presented the time of first operation, age of the patient and lymphadenectomy are not significant. Where as our cohort signifies that complete regression is possible with therapy. This observation may contribute to the discussion about the increasing life expectancy and age-related problems in EOC.[83]

In agreement with previous studies, we observed a higher HR for mucinous, clear cell and non-classified adenocarcinomas in multivariable analyses.[10,83] This finding could be explained by more aggressive biological activity of these tumors. However, examination of such aggressiveness was beyond the scope of this study.

It is not clear whether the better OS we observed in the SCS+PBC group was due to treatment only or also related to tumor biology. However, identifying these factors was beyond the scope of this study. Other studies have indicated a possible association between longer TFI and improved PFS, which may be the case for patients treated with SCS and PBC.[84,85]

Improved survival in our SCS+PBC group does not necessarily mean that survival would have been better for patients in the PBC group if they had first been treated with SCS. The role of SCS in recurrent ovarian cancer treatment has not been clearly defined, and con-clusive evidence is lacking.[13,84,86,87] The studies that indicated improved survival in patients with SCS treat-ment had a prospective design and were criticized for possible selection bias, various types of follow up, use of different diagnostic methods for first recurrence, and different types of chemotherapy given in the SCS group and chemotherapy-alone group, which made the evaluation of the effect of SCS difficult.[84,87,88] In our study, follow up was uniform for all patients, with plausible precision of diagnoses of first and second recurrence. Moreover, chemotherapy was similar in both groups.

This study clearly depicts that surgery is significantly better than chemo for complete regression, where as age at diagnosis or lymphadenectomy or time of first operation no significant effect on complete regression. In our study majority of the patient were diagnosed at stage III of the carcinoma and CT scan was the investigation which signifcantally contributrd in complete regression of the carcinoma. We could also come to a conclusion that therapy and CT scan are two independent factor on the basis of multifactorial analysis. On the basis of survival function graph we can say that survival time after surgery was longer than chemotherapy.

The results from this study will hopefully con-tribute important information about treatment practice in patients with recurring EOC.

The limitation of the study was the period of time of curing and patients monitoring, due to the researcher had 3 years for studying as the house physician. The suggestion was that providing more time for the study, the amount of recurrent cases maybe much more than this current study's patient amount.

5. CONCLUSION

In this study, we obtained statistically significant differences in the efficacy of secondary cytoreductive surgery or chemotherapy alone in patients with recurrent epithelial ovarian cancer. In order to improve the quality of life of patients with recurrent epithelial ovarian cancer, the physical condition of the patient It is advisable to take secondary cytoreductive surgery for patients with recurrent epithelial ovarian cancer. In selected epithelial ovarian cancer patients with no residuals after primary surgery and a recurrent, platinum-sensitive tumor, the complete resection of recurrent tumor at secondary cytoreductive surgery improves progression-free survival and overall survival. Our results suggest that a long treatment-free interval and non-disseminated lesions (three or fewer lesions) on radiological images could be useful predictors for complete resection at secondary cytoreductive surgery.

A thorough check up and investigation is mandatory in all the women who are suspected of the condition. Relevant surgical staging of the disease and pathologic review of the surgical specimen with immunohistochemistry has crucial role in diagnosis of the condition as there were no clue of dedifferentiated endometrial carcinoma prior to biopsy and immunohistochemistry. The positive lymph node metastasis in all the patient with ovarian carcinoma shows the aggressive behavior of the condition.

In the patient with advanced stage disease even multimodality of treatment does not help to improve the quality of life and disease progression. With the further research and new understandings of molecular biology and immunology, more efficacious strategies indicating long term survival and high quality of life are worthy of being expected.

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