Journal of Posthumanism
2025
Volume: 5, No: 7, pp. 2599–2610
ISSN: 2634-3576 (Print) | ISSN 2634-3584 (Online)
posthumanism.co.uk

DOI: https://doi.org/10.63332/joph.v5i7.3107

Clinical Characteristics and Prognosis of Hipec (Hyperthermic intraperitoneal Chemotherapy) plus surgery in different Histological types of Epithelial Ovarian Cancer

Sajid Khan Durrani, FRCP UK[1], Saeed ur Rehman[2], Humariya Heena[3], Tariq Wani[4], Azhar Malik[5], Yousef Alobaisi[6], Sheikh Zafar Ali[7], Yasir A Ahmed[8]

Abstract

Background: Ovarian Cancer also is known as the silent killer is the fifth most common cancer in females worldwide carrying a high mortality rate. In this study, we looked at clinical characteristics and outcomes of different stages and histopathological subtypes of epithelial ovarian cancer in 85 patients, following standard treatment with surgery and chemotherapy. Methods: Patients newly diagnosed with EOC between 2014 to 2017 who were treated with TAHBSO (150 TAHBSO in total with 15 HIPEC) were identified from a medical record maintained database. Surgery consisted of total hysterectomy, bilateral salpingo-oophorectomy, and total/partial omentectomy or HIPEC. The same chemotherapy was given adjuvant post-surgery as per standard guidelines. Results: The median age at the time of diagnosis for patients with Serous tumors was 55 years. Majority i.e. 94.1% of patients were high-grade serous type.The recurrence rate was 75 % for stage 4 patients who had surgery within 42 days of chemotherapy as opposed to 36.6 % of patients treated at an interval of greater than 42 days. This difference was not statistically significant despite slightly worse progression for patients who had a delay in surgery. Conclusions: Our study revealed a non –significant increased risk of recurrence with delaying chemotherapy for greater than 42 days for stage 4 disease while the delay in chemotherapy in stage 3c and lower ovarian cancer did not show any adverse outcome. We have identified the advanced stage of presentation of ovarian cancer being a more relevant factor for recurrence.

Keywords: *Ovarian Cancer, Hyperthermic Intraperitoneal Chemotherapy, Epithelial Ovarian Cancer, Hipec Surgery, Hysterectomy.*

Introduction

The median overall survival of patients with epithelial ovarian cancer has improved over the last three decades with the overall 5-year relative survival rate has increased from 39.3% to 45.4%.[1]

Debulking status determines the outcome of patients with patients following surgery. Complete debulking defined as surgery that leaves behind no visible cancer or no tumors larger than 1 cm

[1] Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia., Email: sdurrani@kfmc.med.sa, (Corresponding Author), ORCID 0000-0002-6591-7341.
[2] Research Center, King Fahad Medical City, Email: saeed.urrehman@nhs.net
[3] Research Center, King Fahad Medical City, Email: heenahumaira1@gmail.com
[4] Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi, Email: twani1@kfmc.med.sa
[5] Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi, Email: drazharmalik394@gmail.com
[6] Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi, Email: drzafa33@yahoo.com
[7] Pathology Clinical Laboratory Medical Administration, King Fahaad Medical City, Riyadh, Saudi Arabia, Email: Yalobaisi@kfmc.med.sa
[8] Senior Lab Tech, Pathology clinical Laboratory Medical Administration, King Fahaad Medical City, Riyadh, Saudi Arabia, Email: alshiqe@gmail.com

(less than 1/2 an inch) shows the best outcome**.**

Winter WE III, et al. J Clin Oncol. 2007; 25:3621-3627 suggested that patients with microscopic residual disease had a PFS of 33 months and Medial OS of 71.9 months, residual disease 0.1-1cms had a PFS of 16.8 and OS of 42.4 months, and residual disease greater than 1 cm had a PFS of 14.1 months and median OS of 35 months.

Five-year relative survival data of Ovarian cancer US depends on the Figo staging with the survival of stage 1 being 90% and stage 4 being 17%. (THE WORLD OVARIAN CANCER COALITION ATLAS ©The World Ovarian Cancer Coalition 2018).

The effect of chemotherapy delays on progression-free and overall survival in the treatment of epithelial ovarian cancer has been documented in several retrospective studies. There have been studies with different timelines of commencement of chemotherapy in relation to surgery with a different outcome. There are at least three phases III randomized trials that have looked at attempted maximal surgical cytoreduction followed by platinum-based primary intraperitoneal chemotherapy in advanced epithelial ovarian cancer demonstrating favorable impact [2–6]

The role of HIPEC in EOC and the optimal chemotherapy regimen(s) are controversial [7]

Chiva *et al*. estimated the average of Overall survival in trials of HIPEC following cytoreduction in the front-line and recurrent settings to be 37.6 and 36.5 months, respectively. These results are comparable to those results noted with standard therapies [8]

Literature Review:

Ovarian cancer is the deadliest gynaecologic malignancy. Approximately 75% of ovarian cancer patients are diagnosed in the advanced stage, when the disease has already spread primarily in the peritoneal cavity.[9]

Epithelial tubo-ovarian cancer is most diagnosed after the disease has spread intraperitoneally. The standard treatment for advanced (FIGO stage III/IV) epithelial tubo-ovarian cancer is primary cytoreductive surgery followed by six cycles of platinum-based intravenous (IV) chemotherapy, or neoadjuvant chemotherapy followed by interval cytoreductive surgery, depending on the individual patient's characteristics and disease spread. [10] Interval surgery is typically performed 3 weeks after the third cycle of chemotherapy, with subsequent cycles restarted within 3-4 weeks of surgery. Women with recurrent disease may be offered surgery followed by chemotherapy, assuming certain eligibility criteria are met, or chemotherapy alone.[11]

Drug delivery directly to the peritoneal surface results in a higher drug concentration than concordantly measured plasma concentrations, limiting systemic toxicity. Intraoperative drug delivery occurs before the formation of intraperitoneal adhesions. Heating increases the cancer's sensitivity to chemotherapy by impairing DNA repair.[12] Mild hyperthermia degrades the BRCA gene, causing a temporary impairment of homologous recombination in tumour cells, limiting their ability to repair double strand breaks in DNA.[13]

HIPEC has been proposed as a particularly effective treatment for chemotherapy-resistant cancer cells that remain after neoadjuvant chemotherapy.[14]

Systemic chemotherapy is the standard treatment for recurrent ovarian cancer (ROC), while surgery's role is still debated. Secondary cytoreductive surgery (SCS) is an option for certain patients who relapse after PDS or NACT/IDS. Selection criteria include platinum sensitivity,

potentially resectable disease, previous complete resection of cancer, localised disease, and absence of ascites in patients with good performance status. [15,16] Two randomised phase III trials (AGO DESKTOP III and SOC-1) compared the efficacy of SCS plus second-line chemotherapy to chemotherapy alone in ROC. The randomised DESKTOP-III trial found that patients undergoing SCS followed by chemotherapy had a higher overall survival rate than those receiving chemotherapy alone, particularly when complete cytoreduction was achieved.[17]

Previous Studies:

Several retrospective studies have suggested that HIPEC improves survival rates in both primary and recurrent ovarian cancer. A randomised trial9 (Interval Debulking Surgery +/− Hyperthermic Intraperitoneal Chemotherapy in Stage III Ovarian Cancer [OVHIPEC-01]) found that HIPEC after interval cytoreductive surgery following neoadjuvant chemotherapy for stage III primary ovarian cancer reduced recurrence and mortality rates.[18,19]

A previous randomised clinical trial demonstrated a significant survival benefit with adjuvant normothermic intraperitoneal/intravenous chemotherapy cycles delivered via a transabdominal catheter. Increased toxicity, logistical challenges, and catheter-related adverse events hampered adoption in clinical practice. [20] The randomised OVHIPEC trial provides additional evidence that adding HIPEC to interval cytoreductive surgery improves recurrence-free and overall survival in patients with stage III ovarian cancer who are ineligible for primary cytoreductive surgery due to extensive intraperitoneal disease.[21]

In 2018, van Driel et al. published a randomised controlled trial of patients with advanced ovarian cancer who had undergone optimal interval debulking surgery after receiving neoadjuvant platinum/taxane chemotherapy. Patients were randomly assigned to receive either surgery alone followed by adjuvant chemotherapy or surgery plus concurrent hyperthermic intraperitoneal chemotherapy (HIPEC) followed by adjuvant chemotherapy. The study found that including HIPEC during interval debulking surgery resulted in a statistically significant benefit in both recurrence-free survival (3.5 months) and overall survival (11.9 months).[22]

Materials and Methods:

Patients newly diagnosed with EOC between 2014 to 2017 who were treated with TAHBSO (150 TAHBSO in total with 15 HIPEC) were identified from a medical record-maintained database, In the end, 85 patients were included after a thorough review of the notes. The reason for exclusion was an incomplete record, continued treatment or follow-up in another hospital and lost to follow up. Only the diagnoses that were confirmed histologically by examination of the biopsy specimens, or by cytological assessment of ascites or pleural effusion are included. Patient charts were reviewed for their demographic information and histological characteristics as well as the time interval between surgery and chemotherapy used, and the outcome was documented. As per the current recommendation, treatment remained the same for all epithelial subtypes.

Surgery consisted of total hysterectomy, bilateral salpingo-oophorectomy, and total/partial omentectomy with/without resection of the metastatic tumor or pelvic and para-aortic lymphadenectomy, or HIPEC. The indication for treatment with TAHBSO and HIPEC was left to the decision of the Tumor Board Indications.

Upfront chemotherapy used was carboplatin AUC 6 and paclitaxel 175mgs/m^2 ,3 cycles on average. The same chemotherapy was given adjuvant post-surgery as per standard guidelines.

Time to surgery after completing neoadjuvant chemotherapy or adjuvant chemotherapy was recorded and was divided into two groups 1) ≤42 days and 2) >42 days as recommended by the society of Gynecology Oncology.

Patient outcomes were collected retrospectively from notes, including the time to progression following upfront surgery. The outcome of different histological Types was recorded.

The dates of recurrence were determined based on clinical examinations, imaging studies, and CA 125 levels.

In this study we looked at the impact of the stage at the presentation on the outcome of Epithelial Ovarian cancer/ fallopian tube/peritoneal cancer and assessed the outcome related to administration of early vs late chemotherapy. We evaluated whether the time between surgery and the initiation of chemotherapy influenced disease-free survival and hence prognosis. Progression-free survival being defined as the time from the end of adjuvant chemotherapy to relapse or progression. The delay was correlated with the change in Progression-free survival.

We identify the amount of time delay in chemotherapy administration during upfront therapy and the impact of delay on patient outcomes, as assessed by progression-free survival. This study was approved by IRB and funded by the research Centre King Fahad Medical City.

Ethical Consideration:

Ethics approval was obtained from the Institutional Review Board at King Fahad Medical City, Riyadh. The manuscript does not report on or involve the use of any animal or human data or tissue.

Results:

The median age at the time of diagnosis for patients with Serous tumors was 55 years. Majority i.e. 94.1% of patients were high-grade serous type, 3.5% being endometroid and the rest of 2.4% were other rare histology's. None of the patients had surgery delayed greater than 3 months.

Patients equal to or lower than stage 3c, treated within 42 days of chemotherapy was 64.9 % and the percentage of patients having had surgery later than 42 days was 36.6 %. Recurrence rates overall were 52.9%. There was no statistically insignificant difference in the outcome for these patients.

Recurrence rate was 75 % for stage 4 Patients who had surgery within 42 days of chemotherapy as opposed to 36.6 % of patients treated at interval of greater than 42 days. This difference was not statistically significant despite slightly worse progression for patients who had a delay in surgery. Since the majority of patients were high grade serous in keeping with the increasing trend of diagnosis of this histological type worldwide, it was not possible to compare the impact of grade on the outcome.

Descriptive Statistics			
Characteristic	Description	Mean ± SD	n (%)
age	Mean ± SD	54.1 ± 13.7	
	Median	55 (19 - 88)	

Time between Surgery and Neoad end	Mean ± SD	41.3 ±17.6
	Median	37 (18 - 82)
Time between Surgery and Start of Adj. chemo	Mean ± SD	42.4 ± 15.6
	Median	40 (18 - 90)
HIPEC	No	72 (84.7)
	Yes	13 (15.3)
Histology	Endometoird	3 (3.5)
	High grade serous	80 (94.1)
	Others	2 (2.4)
Stage	3C and below	59 (69.4)
	4 and Above	26 (30.6)
Neo-adj given	No	44 (51.8)
	Yes	41 (48.2)
Time between Surgery and Neoad end	< 42 days	26 (63.4)
	≥ 42 days	15 (36.6)
Surgery done	No	0 (.0)
	Yes	85 (100.0)
Adjuvant given	No	4 (4.7)
	Yes	81 (95.3)
Time between Surgery and Start of Adj. chemo	< 42 days	49 (60.5)
	≥ 42 days	32 (39.5)
Number of Cycles given	<6	17 (20.5)
	≥ 6	66 (79.5)
Recurrence	No	40 (47.1)
	Yes	45 (52.9)

Taple 1 Descripe the Median Age at the Time of Diagnosis For Patients

The demographic and clinic-pathologic characteristics of the patients in this study are shown above. The median age of diagnosis was years (range,59 -years). The majority of patients had high-grade tumors (89%) with the remainder having endometriod (5%), remaining (6%) rare histology's.

Correlation between Stage of Disease and the Studied Characteristics				
Characteristic	Description	3C and below	4 and Above	p value
Histology	Endometoird	2 (3.4)	1 (3.8)	0.635
	High grade serous	55 (93.2)	25 (96.2)	
	Others	2 (3.4)	0 (.0)	
Neo-adj given	No	31 (52.5)	13 (50.0)	0.829
	Yes	28 (47.5)	13 (50.0)	
Surgery done	No	0 (.0)	0 (.0)	1
	Yes	59 (100.0)	26 (100.0)	

Time between Surgery and Neoad end	<42	18 (64.3)	8 (61.5)	0.865
	≥42	10 (35.7)	5 (38.5)	
Adjuvant given	No	3 (5.1)	1 (3.8)	0.804
	Yes	56 (94.9)	25 (96.2)	
Number of Cycles given	<6	12 (21.1)	5 (19.2)	0.849
	≥6	45 (78.9)	21 (80.8)	
Time between Surgery and Start of Adj. chemo	<42	37 (66.1)	12 (48.0)	0.124
	≥42	19 (33.9)	13 (52.0)	
Recurrance	No	31 (52.5)	9 (34.6)	0.127
	Yes	28 (47.5)	17 (65.4)	
Time between Surgery and Neo-Adj or Adj	<42	37 (64.9)	12 (46.2)	0.107
	≥42	20 (35.1)	14 (53.8)	

Table 2 Correlation between Stage of Disease and the Studied Characteristics

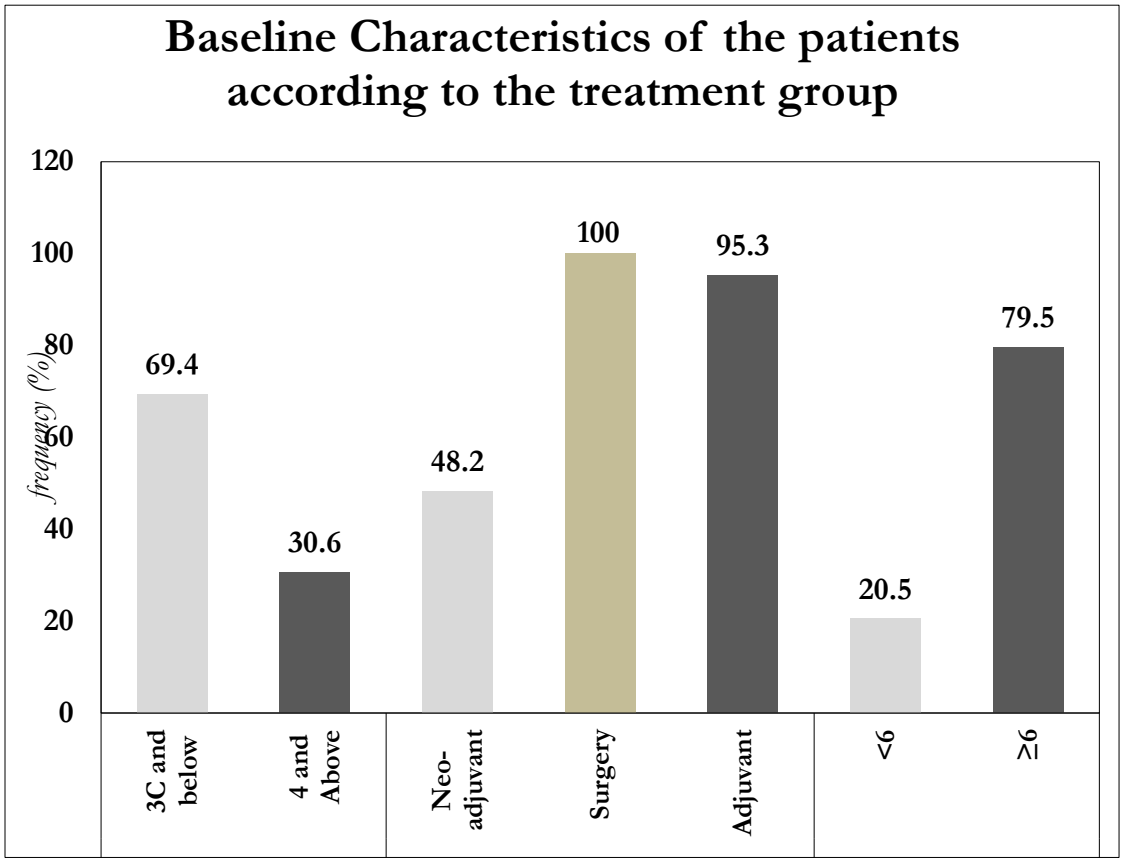

Fig1 Describe the Stage of Disease ,Treatment Modality and Number of Cycles Given

Stage of Disease vis-a-vis the Recurrence w.r.t. Time between Surgery and Chemotherapy							
Characteristic	Time (day)	3C and below			4 and Above		
		No recurrence	**Recurrence**	**Total**	**No recurrence**	**Recurrence**	**Total**
Time between Surgery and Neo-adjuvant end	<42	6 (33.3)	12 (66.7)	18 (64.3)	2 (25.0)	6 (75.0)	8 (61.5)
	≥42	5 (50.0)	5 (50.0)	10 (35.7)	4 (80.0)	1 (20.0)	5 (38.5)
Time between Surgery and Start of Adjuvant chemo	<42	16 (43.2)	21 (56.8)	37 (66.1)	6 (50.0)	6 (50.0)	12 (48.0)
	≥42	13 (68.4)	6 (31.6)	19 (33.9)	2 (15.4)	11 (84.6)	13 (52.0)
Time between Surgery and Neo-adjuvant or Adjuvant	<42	16 (43.2)	21 (56.8)	37 (64.9)	6 (50.0)	6 (50.0)	12 (46.2)
	≥42	13 (65.0)	7 (35.0)	20 (35.1)	3 (21.4)	11 (78.6)	14 (53.8)

Table 3 Stage of Disease vis-a-vis the Recurrence w.r.t. Time between Surgery and Chemotherapy

For patients operated within 42 days, recurrence amongst the Stage 4 subjects was observed in 50% cases, while 56.8% of recurrences were observed among 3C and below stages. Similarly; Recurrence amongst Stage 4 or more in the ≥42-day time interval subjects were observed in 78.6% cases, and 35.0% among the 3C and below the stage of disease had a recurrence. The difference was not statistically significant.

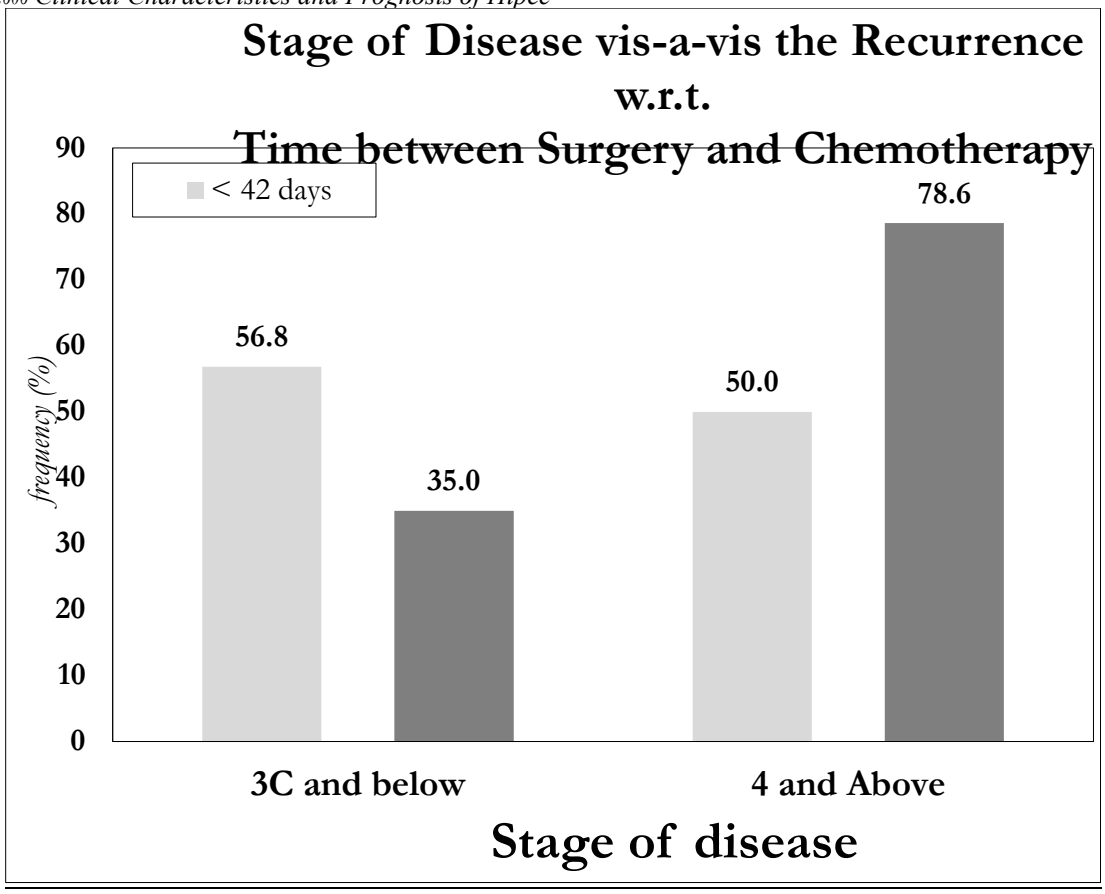

Fig 2 Stage of Disease

Discussion:

Majority of Epithelial Ovarian Cancer are serous tumors which are highly chemosensitive, and appears to affect results. **As per Saudi cancer registry there were 409 new cases diagnosed in 2018 .Globocan 2018**

One of the strongest predictors of outcome for patients with High grade serous carcinoma is surgical cytoreduction. Using neoadjuvant chemotherapy has been investigated in many studies as an alternative treatment option to reduce tumour burden before surgery in order to maximize the chances of complete cytoreduction.

Quality of surgical staging is an important determinant of adjuvant chemotherapy and Disease stage is a prognostic factor that influences the choice of therapy.

Histopathology provides prognostic indicators which ascertains treatment planning for women diagnosed with epithelial ovarian cancer. Endometroid histology has shown to have the best Progression free survival of around 24.8months while serous carcinoma PFS of 16.9 months, clear cell with a PFS of 11.4 months and mucinous PFS being 10.5. Median Overall survival was 56 ,45.1,24.0,14.8 months accordingly .[23] The histologic types of EOC are diagnosed based on the morphological criteria .[24].

Neoadjuvant chemotherapy followed by interval debulking has shown not to be inferior to standard treatment of primary surgery followed by chemotherapy[25] Delay in timeliness of chemotherapy affects the outcome. Quality measure suggested by Society of Gynecologic Oncology is to give chemotherapy within 42 days of cytoreductive surgery in patients with epithelial ovarian cancer.(sgo.org).

Using SEER-Medicare data on patients with advanced Epithelial Ovarian cancer who underwent radical cytoreductive surgery, Wright et al looked at delays in the time to initiation of chemotherapy after surgery.[26] Results suggested that giving chemotherapy twelve weeks or more after surgery resulted in a significant increased risk of death (HR = 1.32, 95% CI:1.07–1.64).

Similarly, Dataset analysis including **patients** between 1998–2011 using the National Cancer Database evaluated delay in initial chemotherapy administration after surgery. [27] .Delay was defined as delay in time to first administration of chemotherapy more than 28 days from surgery. Study found that initiation of chemotherapy after 36 days was significantly associated with a 14% increased risk of death. The 25–29-day interval had the weakest association with death.

In the Gog 208, post Hoc analysis, the median time to surgery and chemotherapy was 31 days. The analysis revealed that risk of death increased sharply if chemotherapy was initiated more than 25 days after surgery; effect was most pronounced for patients with R0 cytoreduction. A meta-analysis by Mahner et al reviewed outcome data for 3326 patients from three phase III randomized studies of primary therapy for ovarian cancer by the AGO-OVAR and GINECO [28], following complete surgical resection, patients who had Delay in chemotherapy was associated with earlier disease recurrence and significantly reduced Overall survival.

There have been inconclusive results about the timing of initiation of chemotherapy following surgery with some studies[29,30,31] suggesting that shorter the initiation time of adjuvant chemotherapy better the prognosis of ovarian cancer patients. Other studies[31,33,34] did not seems to have a positive predictive value and does not draw a clear conclusion about this association.

In one large study involving 668 patients 59.1% of patients received chemotherapy within 42 days of surgery.[35]

In our population of patients 57.6 % had chemotherapy within 42 days of surgery.

Study Limitations:

Our study is limited since ovarian cancer is not common cancer, and it is difficult to get many epithelial ovarian cancer patients which would make the data more powerful.

It involves different modalities like chemotherapy and surgery which were given in different hospitals involving private hospitals and hence comprehensive data collection and follow-up was cumbersome and limited our numbers further.

Conclusion:

Our study revealed a non –significant increased risk of recurrence with delaying chemotherapy for greater than 42 days for stage 4 disease while the delay in chemotherapy in stage 3c and lower ovarian cancer did not show any adverse outcome. We have identified the advanced stage of presentation of ovarian cancer being a more relevant factor for recurrence as opposed to delay of chemotherapy in early-stage disease and recommend the early surgical procedure for stage 4 disease. Although we did not look at the outcome for survival but in wake of the current corvid

pandemic, this study gives us an insight to priorities stage 4 epithelial Ovarian cancer for surgery and is reassuring that a delay of surgery less the 3 months does not cause any statistically significant worsening of progression-free survival.

Authors' contributions:

S.D and Y.O. designed the study. All Authors Collect and analysed the data. Y.A. review the manuscript and do the publication S.D and Y.O. wrote the paper with input from all authors.

Acknowledgment

- We are expressing our gratitude and appreciation to Research Center, King Fahad Medical City for providing the research grant.
- We would like to extend our thanks to all individuals who provided help and assistance to the researchers during the project.

References

J Cancer. 2018; 9(19): 3548–3556.Published online 2018 Sep 8. doi: 10.7150/jca.26300

National Cancer Institute. NCI Clinical Announcement on Intraperitoneal chemotherapy for ovarian cancer. http://ctep.cancer.gov/highlights/docs/clin annc_010506.pdf.

Armstrong DK, Bundy B, Wenzel L et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med 2006;354:34–43.

Tewari D, Java JJ, Salani R et al. Long-term survival advantage and prognostic factors associated with intraperitoneal chemotherapy treatment in advanced ovarian cancer: A gynecologic oncology group study. J Clin Oncol 2015;33:1460–1466.

Elit L, Oliver TK, Covens A et al. Intraperitoneal chemotherapy in the first-line treatment of women with stage III epithelial ovarian cancer: A systematic review with metaanalyses. Cancer 2007;109: 692–702.

Wright AA, Cronin A, Milne DE et al. Use and effectiveness of intraperitoneal chemotherapy for treatment of ovarian cancer. J Clin Oncol 2015;33:
2841–2847.

Coccolini F, Campanati L, Catena F, et al. Hyperthermic intraperitoneal chemotherapy with cisplatin and paclitaxel
in advanced ovarian cancer: a multicenter prospective observational study. J Gynecol Oncol 2015;26:54-61.

Chiva LM, Gonzalez-Martin A. A critical appraisal of hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of advanced and recurrent ovarian cancer.

Siegel R.L., Miller K.D., Fuchs H.E., Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7–33. doi: 10.3322/caac.21708.

Colombo N, Sessa C, du Bois A, Ledermann J, McCluggage WG, McNeish I, et al. ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. Int J Gynecol Cancer 2019; 29: 728–760.

Vergote I, Coens C, Nankivell M, Kristensen GB, Parmar MKB, Ehlen T, et al. Neoadjuvant chemotherapy versus debulking surgery in advanced tubo-ovarian cancers: pooled analysis of individual patient data from the EORTC 55971 and CHORUS trials. Lancet Oncol 2018 Dec;19(: 1680–7.

Harter P, Sehouli J, Vergote I, Ferron G, Reuss A, Meier W, et al. DESKTOP III Investigators. Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer. N Engl J Med 2021 Dec

2;385: 2123–31.
Arjona-Sánchez A, Espinosa-Redondo E, Gutiérrez-Calvo A, Segure-Sampedro JJ, Perez Viejo E, Concepcion-Martin V, et al. Grupo Español de Carcinomatosis Peritoneal. Efficacy and Safety of Intraoperative Hyperthermic Intraperitoneal Chemotherapy for Locally Advanced Colon Cancer: A Phase 3 Randomized Clinical Trial. JAMA Surg 2023 Jul 1;158: 683–91.
Kim SI, Kim JH, Lee S, Cho H, van Driel WJ, Sonke GS, et al. Hyperthermic intraperitoneal chemotherapy for epithelial ovarian cancer: A meta-analysis. Gynecol Oncol 2022 Oct 20:S0090-8258(22)01887-X.
Baek, M.H.; Park, E.Y.; Ha, H.I.; Park, S.Y.; Lim, M.C.; Fotopoulou, C.; Bristow, R.E. Secondary Cytoreductive Surgery in Platinum-Sensitive Recurrent Ovarian Cancer: A Meta-Analysis. J. Clin. Oncol. 2022, 40, 1659–1670.
Harter, P.; Sehouli, J.; Vergote, I.; Ferron, G.; Reuss, A.; Meier, W.; Greggi, S.; Mosgaard, B.J.; Selle, F.; Guyon, F.; et al. DESKTOP III Investigators. Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer. N. Engl. J. Med. 2021, 385, 2123–2131.
Shi, T.; Zhu, J.; Feng, Y.; Tu, D.; Zhang, Y.; Zhang, P.; Jia, H.; Huang, X.; Cai, Y.; Yin, S.; et al. Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): A multicentre, open-label, randomised, phase 3 trial. Lancet. Oncol. 2021, 22, 439–449.
Cowan RA, O'Cearbhaill RE, Zivanovic O, Chi DS. Current status and future prospects of hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) clinical trials in ovarian cancer. Int J Hyperthermia. 2017;33(5):548-553. doi:10.1080/02656736.2017.1283066
Vergote I, Harter P, Chiva L. Hyperthermic intraperitoneal chemotherapy does not improve survival in advanced ovarian cancer. Cancer. 2019;125(suppl 24):4594-4597. doi:10.1002/cncr.32496.
J.L. Walker, M.F. Brady, L. Wenzel. Randomized trial of intravenous versus intraperitoneal chemotherapy plus bevacizumab in advanced ovarian carcinoma: an NRG Oncology/Gynecologic Oncology Group study. JCO, 37 (2019), pp. 1380-90. doi:10.1200/JCO.18.01568.
W.J. van Driel, S.N. Koole, K. Sikorska. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med, 378 (2018), pp. 230-40. doi:10.1056/NEJMoa1708618.
W.J. van Driel, S.N. Koole, K. Sikorska, J.H. Schagen van Leeuwen, H.W.R. Schreuder, R.H.M. Hermans, I. de Hingh, J. van der Velden, H.J. Arts, L. Massuger, A.G.J. Aalbers, V.J. Verwaal, J.M. Kieffer, K.K. Van de Vijver, H. van Tinteren, N.K. Aaronson, G.S. Sonke, Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer, N Engl J Med 378(3) (2018) 230– 240.
Winter WE III, et al. J Clin Oncol. 2007;25:3621-3627.
(1971; Tavassoli, 2003)
The phase III EORTC 55971 trial (N Engl J Med. NCIC
Wright JD, Herzog TJ, Neugut AI, Burke WM, Lu YS, Lewin SN, et al. Effect of radical cytoreductive surgery on omission and delay of chemotherapy for advanced-stage ovarian cancer. Obstet Gynecol. 2012;120(4):871–81. Epub 2012/09/22. pmid:22996105.
Seagle BL, Butler SK, Strohl AE, Nieves-Neira W, Shahabi S. Chemotherapy delay after primary debulking surgery for ovarian cancer. Gynecologic oncology. 2017;144(2):260–5. Epub 2016/12/03. pmid:27908531.
Mahner S, Eulenburg C, Staehle A et al. Prognostic impact of the time interval between surgery and chemotherapy in advanced ovarian cancer: analysis of prospective randomised phase III trials. Eur J Cancer 2013; 49: 142–149. [PubMed] [Google Scholar]
Hofstetter, G. et al. The time interval from surgery to start of chemotherapy significantly impacts prognosis in patients with advanced serous ovarian carcinoma - analysis of patient data in the

prospective OVCAD study. Gynecol Oncol 131, 15–20 (2013).CAS,Article,PubMedGoogle Scholar
Mahner, S. et al. Prognostic impact of the time interval between surgery and chemotherapy in advanced ovarian cancer: analysis of prospective randomised phase III trials. Eur J Cancer 49, 142–9 (2013).ADS,CASArticle,PubMedGoogle Scholar
Wright, J. D. et al. Effect of radical cytoreductive surgery on omission and delay of chemotherapy for advanced-stage ovarian cancer. Obstet Gynecol 120, 871–81 (2012).
Feng, Z., Wen, H., Bi, R., Yang, W. T. & Wu, X. H. Prognostic impact of the time interval from primary surgery to intravenous chemotherapy in high grade serous ovarian cancer. Gynecol Oncol 141, 466–470 (2016).ArticlePubMedGoogle Scholar
Gadducci, A. et al. Relationship between time interval from primary surgery to the start of taxane- plus platinum-based chemotherapy and clinical outcome of patients with advanced epithelial ovarian cancer: results of a multicenter retrospective Italian study. J Clin Oncol 23, 751–8 (2005).CASArticlePubMedGoogle Scholar
Flynn, P. M., Paul, J. & Cruickshank, D. J. Does the interval from primary surgery to chemotherapy influence progression-free survival in ovarian cancer? Gynecol Oncol 86, 354–7 (2002).ArticlePubMedGoogle Sch
Time to chemotherapy in ovarian cancer: Compliance with ovarian cancer quality indicators at a National Cancer Institute-designated Comprehensive Cancer Center
Adam C ElNaggar 1, Erinn M Hade 2, David M O'Malley 3, Margaret I Liang 3, Larry J Copeland 3, Jeffrey M Fowler 3, Ritu Salani 3, Floor J Backes 3, David E Cohn 3
Affiliations expandPMID: 30282591.DOI: 10.1016/j.ygyno.2018.09.014