



STUDY OF RECURRENCE AND SITE OF RECURRENCE IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CANCER - A SINGLE CENTER EXPERIENCE

Oncology

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ABSTRACT

OBJECTIVE – Study of recurrence and pattern of recurrence in Stage III epithelial ovarian cancer.

METHODOLOGY – A prospective observational, study was conducted at a tertiary hospital in Bangalore, India from April 2017 to April 2019. Informed and written consent was taken before including the patient in the study. All patients diagnosed with stage III epithelial ovarian with no residual disease following cytoreductive surgery (primary, interval and secondary) with or without Hyperthermic Intraperitoneal Chemotherapy (HIPEC) were included in the study. Patients were followed every 3-6 months up to maximum period of 24 months from the date of surgery. Last date of follow up was on 30/04/19. During follow up patient symptoms, physical examination and serum CA-125 were recorded to detect recurrence. If patient symptoms, physical examination and rising serum CA-125 are suggestive of recurrence, imaging in form of CECT abdomen/ PETCT was done for detection of recurrence. Patients were monitored for two types of recurrence. Biochemical recurrence defined as rising CA-125 in absence of clinical evidence of recurrence either by physical examination or by imaging. Clinical recurrence defined as recurrence in any part of body noted on physical examination or imaging and then proving it by biopsy with or without rise in serum CA-125. Site of first recurrence was recorded.

RESULTS- A total of 84 patients were included in the study. 45 patients underwent interval, 25 patients underwent primary and 14 patients underwent secondary cytoreductive surgery. Mean duration of follow up was 18.25 months. 4 patients lost follow up. 2 patients died following surgery. Recurrence was noted in 14 patients (16.66%). Clinical recurrence was noted in 13 patients (15.47%) and biochemical recurrence was noted in 1 patient (1.19%). 8 patients had recurrence in peritoneal cavity (57.14%). 1 patient each had recurrence right inguinal lymph node, para-aortic lymph node+ peritoneum, left iliac lymph node, left supraclavicular lymph node and left inguinal lymph node.

CONCLUSION – In this study clinical recurrence was more common than biochemical recurrence. Peritoneal cavity was most common site for recurrence. This study shows importance of optimal cytoreductive surgery in preventing recurrence in carcinoma ovary as peritoneal cavity is most common site of recurrence.

KEYWORDS

Epithelial Ovarian Cancer, Cytoreductive surgery, Recurrence.

INTRODUCTION

Ovarian cancer is known to have high recurrence. Recurrence is about 25% in early-stage ovarian cancer (FIGO stage I and II) and around 80% in advanced ovarian cancer (FIGO stage III and IV) (1). Most patients with advanced ovarian cancer have recurrence within next 2 years after treatment (2,3). Peritoneum is the most common site of recurrence (4). Optimal cytoreductive surgery leaving behind no residual disease in best way to prevent recurrence hence improving survival with or without use of intraperitoneal chemotherapy (5). Recurrence and pattern of recurrence was noted in this study in FIGO stage III epithelial ovarian cancer.

METHODOLOGY

A prospective observational study was conducted at a tertiary hospital at Bangalore between April 2017 to April 2019. All patients diagnosed with stage III epithelial ovarian cancer who underwent primary, interval and secondary cytoreductive surgery with or without HIPEC were included in the study. Type of surgery was decided by the surgeon under whom patient was admitted. Only patients for underwent optimal cytoreductive surgery i.e., no residual disease noted following surgery were included in the study. Informed and written consent was taken before including the patient in the study. Semi open technique is used for HIPEC procedure. Peritoneal dialysis solution was used for HIPEC procedure. The mean temperature was set at 41.5 degree Celsius. Duration of HIPEC was for 90 minutes. Most common chemotherapy drug used was Cisplatin at a dose 75-100mg/m² for platinum sensitive cases. Combination of Cisplatin and Adriamycin was used for platinum resistant cases.

Patients were followed every 3-6 months up to maximum period of 24 months from the date of surgery. Follow up all patients was done up to date 30/04/19. During follow up patient symptoms, physical examination and Serum CA-125 were recorded. If patient symptoms, physical examination and rising serum CA-125 are suggestive of recurrence, imaging in form of CECT abdomen/ PETCT was done for detection of recurrence. Patients were monitored for two types of recurrence. One was biochemical recurrence defined as rising CA-125 in absence of clinical evidence of recurrence either by physical examination or by imaging. Clinical recurrence defined as recurrence

in any part of body noted on physical examination or imaging (CECT abdomen and pelvis/ PETCT and then proving it by biopsy with or without rise in S.CA-125. Site of first recurrence was recorded.

RESULTS

1) Primary, Interval And Secondary Cytoreductive Procedures Done In This Study

Table 1- Showing number of patients who underwent interval, primary and secondary cytoreductive surgery.

TIMING OF SURGERY	TOTAL NUMBER OF PATIENTS	PERCENTAGE OF PATIENTS
INTERVAL	45	53.57%
PRIMARY	25	29.76%
SECONDARY	14	16.66%
TOTAL	84	100%

2) Clinical And Biochemical Recurrence Noted In This Study

Table 2- Showing biochemical and clinical recurrence noted during follow up.

RECURRENCE	CLINICAL	PERCENTAGE OF RECURRENCE
CLINICAL	13	15.47%
BIOCHEMICAL	1	1.19%
TOTAL	14	16.66%

3) Site Of Clinical Recurrence Noted In This Study

Table3 – Showing site of clinical recurrence.

SITE OF PHYSICAL RECURRENCE	NUMBER OF PATIENTS	PERCENTAGE
Peritoneal cavity	8	57.14%
Right inguinal lymph node	1	7.1%
Para-aortic lymph node+ peritoneum	1	7.1%
Left iliac lymph node	1	7.1%

Left supraclavicular lymph node	1	7.1%
Left inguinal lymph node	1	7.1%
Total number of patients with clinical recurrence	13	92.85%

DISCUSSION

A total of 84 patients were included in the study. 45 patients underwent interval, 25 patients underwent primary and 14 patients underwent secondary cytoreductive surgery. Mean duration of follow up was 18.25 months. 4 patients did not follow up. 2 patients died following surgery. Recurrence was noted in 14 patients (16.66%). Clinical recurrence was more than biochemical recurrence in this study. Clinical recurrence was noted in 13 patients (15.47 %) and biochemical recurrence was noted in 1 patient (1.19%). 8 patients had recurrence in peritoneal cavity (57.14%). Finding of this is similar to study done by Amate et al. where peritoneal recurrence was noted in 75% of patients. Next common type of recurrence following peritoneal recurrence was nodal recurrence (28.4%). 1 patient each had recurrence right inguinal lymph node, para-aortic lymph node+ peritoneum, left iliac lymph node, left supraclavicular lymph node and left inguinal lymph node. This finding also correlates with study done by Amate et al. where nodal recurrence was noted in 38% of patients. The main risk factors for peritoneal recurrences are 1) leaving behind gross residual disease following cytoreduction 2) Even after extensive cytoreduction and gross disease removal, microscopic disease is left behind. Study done by Van Driel et al. showed improvement in overall survival by use of cytoreductive surgery + HIPEC over cytoreductive surgery alone in primary carcinoma ovary in OVOHIPEC1 study (6). Bois et al. showed improvement in overall survival by use secondary cytoreductive and chemotherapy over chemotherapy alone in platinum sensitive recurrent carcinoma ovary (DESKTOP III study) (7). Spiliotis showed in overall survival by use of secondary cytoreductive surgery and HIPEC in platinum resistant recurrent ovarian cancer (8).

CONCLUSION

Clinical recurrence was more common than biochemical recurrence. Peritoneal cavity was most common site for recurrence. This study shows importance of optimal cytoreductive surgery i.e., leaving behind no residual disease in preventing recurrence in carcinoma ovary. Preventing recurrence which improves overall survival in carcinoma ovary. Limitation of this study was 1) Single institution study 2) Short duration of study 3) Only FIGO stage III patients included in the study 4) Recurrence free survival and overall survival could not be calculated.

REFERENCES

- 1) Simone Garzon Antonio Simone Laganà, Jvan Casarin, Ricciarda Raffaelli, Antonella Cromi, Massimo Franchi et. al. Secondary and tertiary ovarian cancer recurrence: what is the best management? *Gland Surgery* 2020;9 (4): 1118-1129.
- 2) Andreas du Bois 1, Alexander Reuss, Eric Pujade-Lauraine, Philipp Harter, Isabelle Ray-Coquard, Jacobus Pfisterer. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). *Cancer*. 2009; 115:1234-1244.
- 3) Ignace Vergote 1, Claes G Tropé, Frédéric Amant, Gunnar B Kristensen, Tom Ehlen, Nick Johnson, René H M Verheijen et. al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N. Engl. J. Med.* 2010; 363:943-953.
- 4) Pascale Amate, Cyrille Huchon, Anne Lucie Dessapt, Chérizade Bensaid, Jacques Medioni, Marie-Aude Le Frère Belda et al. Ovarian Cancer: Sites of recurrence. *Int. J. Gynecol. Cancer* 2013;23: 1590-1596
- 5) Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol.* 2002 Mar 1;20(5):1248-59.
- 6) J. van Driel, S.N. Koole, K. Sikorska, J.H. Schagen van Leeuwen, H.W.R. Schreuder, R.H.M. Hermans et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer. *New England Journal of Medicine* 2018; 378:230-40.
- 7) Andreas Du Bois, Ignace Vergote, Gwenaél Ferron, Alexander Reuss, Werner Meier, Stefano Greggi et. al. Randomized Controlled Phase III Study Evaluating the Impact of Secondary Cytoreductive Surgery in Recurrent Ovarian Cancer: Final analysis of AGO DESKTOP III/ENGOT Ov20. *Journal of Clinical Oncology* 2020;38:6000-6000.
- 8) Spiliotis J., Halkia E., Lianos E., Kalantzi, N., Grivas A., Efsthathiou E. et al. Cytoreductive surgery and HIPEC in recurrent epithelial ovarian cancer: A prospective randomized phase III study. *Annals of Surgical Oncology* 2015; 22:1570–1575.