Role of Omentectomy and Random Peritoneal Biopsies in the Upstaging of Apparent Early Stage Epithelial Ovarian Cancer

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Summary

Among gynecologic cancers, ovarian cancer (OC) is the one which poses major health concern. OC commonly spreads to the abdominal cavity and forms implant tumors through peritoneal circulation. In order to determine optimal therapy for clinical early stage OC, definitive staging—that is, surgical staging—is vital. Peritoneal washing, ovary removal, hysterectomy, lymphadenectomy, omentectomy, and peritoneal biopsy are all surgical staging techniques. It is unclear whether peritoneal biopsies and omentectomy should be always performed during thorough surgical staging. As a result, we undertook this study to assess if omentectomy and random peritoneal biopsies should be performed routinely for all patients with clinical early-stage EOC. All participants who were 18 years or older and had an apparent early-stage epithelial OC underwent surgical staging and treatment. The subjects' medical records were reviewed for demographics including age, BMI, gravidity, parity, presenting complaint, previous history, CT reports, as well as tumour histology and grade. Operative notes were reviewed. Of these 72 cases, 20 cases revealed with borderline pathology in final histopathology report. Histology for EOC were serous with 26 (36%) cases followed by mucinous 16 (22%) cases and least with clear cell carcinoma with 1 (1%) case. All cases underwent ascitic fluid or peritoneal fluid cytology analysis. Out of these, 17 (24%) cases came positive. Four (12%) cases had positive peritoneal biopsies. Among these cases, 13 (18%) cases show omental occult metastasis. In our study among 46 cases of clinical stage 1a, 6 cases were upstaged due to positive ascitic fluid or peritoneal fluid cytology, 3 cases due to ovarian surface involvement, 2 cases due to fallopian tube involvement, 1 due to positive pelvic peritoneal biopsy and 5 cases due to positive omental metastasis. In Stage 1b, 14 cases were upstaged. Only one surgical spill case was turned up with 3a omental metastasis. 2b stage were upstaged with 1 case to 3a stage. Due to few positive outcomes in biopsies, peritoneal biopsies do not appear to be beneficial for early stage epithelial ovarian cancer. To verify and build on our findings, more study with a bigger sample size is required.

Keywords: Epithelial ovarian cancer, Omentectomy, Peritoneal biopsies, Surgical staging

Introduction

Ovarian cancer (OC) is the leading cause of death in women with gynecologic cancers. According to GLOBOCAN 2020, an estimated 45,701 new OC diagnoses and 32,077 deaths occurred in India.[1] Various research have looked into ovarian cancer subgroups. According to studies, epithelial origin accounts for up to 90% of all OC, whereas non-epithelial origin accounts for the remainder.[2] Approximately half of the OCs were discovered at an advanced stage. The prognosis for advanced-stage OC is poorer than for early-stage OC.[3,4] Through peritoneal circulation, ovarian cancer frequently spreads to the abdominal cavity and develops implant tumours.[5] These implant tumours are important prognostic indicators because they suggest a higher risk of recurrence and mortality as compared to OC without abdominal implant tumours. Implant tumours are also a key factor in determining whether or not additional treatment is required.[6-8] Patients are upstaged to IIIA if histologically verified microscopic seeding of the abdominal peritoneal surfaces is discovered.[4] Women with stage IIIA epithelial ovarian cancer have a worse prognosis than women with earlier stages of the disease, and they require more intensive treatment, such as systemic or intraperitoneal chemotherapy, to optimize their chances of survival.[5]

As a result, definitive staging—that is, surgical staging—is required to determine treatment for clinically early stage OC. Peritoneal washing, ovary removal, hysterectomy, lymphadenectomy, omentectomy, and peritoneal biopsy are all surgical staging techniques. Cytological analysis, peritoneal biopsy, and omentectomy are used to assess the spread of OC through peritoneal fluid circulation.[9-12]

We conducted this study about OC to evaluate whether omentectomy and random peritoneal biopsies should be routinely performed for all patients with clinical early-stage EOC.

Materials and Methods

The study included participants aged 18 or older who received surgical staging and treatment for an apparent early-stage epithelial ovarian cancer reported at our tertiary care Gujarat Cancer Research and Institute in Ahmedabad between January 2017 and December 2020. These subjects were identified and data was collected retrospectively through hospital records.

Patients' demographics, such as age at diagnosis, BMI, gravidity, parity, presenting ailment, previous history, CT/MRI results, and tumour histology and grade, were reviewed in the subjects' medical records. In addition, the subjects' operative notes were examined for information on intraoperative findings for the extent of disease spread in the pelvis and apparent stage, as well as whether the omentum and peritoneal surfaces in question appeared to have metastatic disease, and whether biopsies were of normal tissue (random biopsy) or of abnormal-appearing tissue (targeted biopsy).

The subjects had an epithelial ovarian cancer diagnosed with complete surgical staging, culminating in a final stage IA to IIIA. Subjects with obvious abdominal disease, as well as those with positive lymph nodes, were excluded. The study enrolled a total of 72 patients.

MSEXCEL was used to tabulate demographic and clinicopathological patient characteristics, as well as if an omentectomy and multiple biopsies were conducted on all patients. Histopathologic characteristics were presented in percentages, including cytology report, peritoneal biopsy results, omentum metastases and stage.

Result

During the period of January 2017 to December 2020, total of 166 primary staging surgeries were conducted at our institute. Out of these 72 were exclusively for EOC and among these 72 cases, 20 (28%) cases were diagnosed with borderline in final histopathology report. The most common histology for EOC were serous with 26 (36%) cases followed by mucinous 16 (22%) cases and least with clear cell carcinoma with 1 (1%) case.

All cases underwent ascitic fluid or peritoneal fluid cytology analysis. Among these 17 (24%) cases came positive.

Random peritoneal biopsies were done in 33 cases. Out of these only 4 (12%) cases had positive peritoneal biopsies. Among these 4 cases, 2 cases with

Table 1: Clinicopathologic Characteristics N=72

	No.	**%**
Histology		
Serous	26	36
Endometroid	05	07
Mucinous	16	22
Clear cell	01	01
Mixed	02	03
Undifferentiated	02	03
Other (borderline)	20	28
Cytologypositive	17	24
Peritoneal Biopsies positive (N=33)	04	12
Omentum positive	13	18

Table 2: Upstaging Characteristics

Intraop (clinical staging)		Final stage (surgicopathological staging)					
		1a	1b	1c	2a	2b	3a
1a	46	29		9	2	1	5
1b	19		4	6	1		7
1c	2			1			1
2a	1				1		2
2b	4					3	1

Table 3: Characteristics of patients upstaged due to peritoneal biopsies and omentectomy

Series	Age (years)	Upstaging site	Intraop stage (clinical stage)	Final stage (surgicohistological stage)	Histology	Cytology
1	53	Omentum	1a	3a	Endometroid	Positive
2	50	Omentum	1b	3a	Serous	Positive
3	62	Pelvic peritoneum	1a	2b	Endometroid	Negative
4	56	Omentum	1b	3a	Serous	Positive
5	45	Omentum	1b	3a	Serous	Negative
6	41	Omentum	1b	3a	Serous	Positive
7	65	Omentum	1a	3a	Serous	Negative
8	45	Omentum	1b	3a	Serous	Positive
9	54	Omentum	1b	3a	Serous	Positive
10	45	Omentum	1c	3a	Serous	Positive
11	56	Omentum	1a	3a	Serous	Positive
12	50	Omentum	1b	3a	Serous	Suspicious
13	44	Omentum	2b	3a	Serous	Positive
14	55	Bladder peritoneum, Omentum	1a	3a	Serous	Negative

suspected nodules from peritoneum came out to be positive and remaining 2 were from normal pelvic and bladder peritoneal biopsies. Nodules which were became positive were from Pouch of Douglas (POD) and bladder peritoneum. Out of 72 cases, 13 (18%) cases were positive for omental occult metastasis.

Distribution of upstaged patient and a comparison of intra operative and final stages is shown in Table 2. Of these, the patients who seems to be stage 1a were upstaged in final histopathology report were 17 cases. Among 17 cases 6 were upstaged due to positive ascitic fluid or peritoneal fluid cytology, 3 due to ovarian surface involvement, 5 cases due to positive omental metastasis, 2 cases due to same side fallopian tube involvement and 1 case due to positive pelvic peritoneum biopsy. In Stage 1b, 14 cases were upstaged to stage 1c, 2a, 3a were 6, 1, 7 respectively. Only one surgical spill case was turned up with 3a omental metastasis. 2b stage were upstaged with 1 case to 3a stage. The characteristics of patients upstaged following random peritoneal biopsies and omentectomy is shown in Table 3.

Discussion

Occult metastasis occurs in only a small percentage of women with clinically obvious early stage ovarian cancers. Diagnosis of occult metastasis helps in tailoring adjuvant chemotherapy, which can improve survival of patients.[13] These metastases are best detected through systematic surgical staging. All women with obvious early-stage ovarian cancers should undergo omentectomy and random peritoneal biopsies. Random peritoneal biopsies should be taken from pelvic, cul-de-sac, both paracolic gutters, bladder peritoneum and intestinal mesentery, if no visible disease identified.[14]

According to Shroff et al study, out of 122 cases 5 (4%) had microscopic metastasis to omentum.[13] While in Powless et al out of 196 cases 4 (2%) had positive omental metastasis.[15] Ayhan et al had 8 (5%) cases showing peritoneal biopsy and/ or omentum positive for metastasis.[16] In our study, all patient underwent omentectomy. Out of 72 cases 13 (18%) had positive omental metastasis in our study. According to Gracia- Soto et al upstaging is common after peritoneal, omental or adhesion biopsy.[17] Metastatic disease in the omentum has been observed in all from 0% to 11% of cases.[18] This result is very similar to our study. As per recent studies by Shroff et al and Powless et al the omentum is the most common site of concealed metastasis. Hence when peritoneal biopsy is not accessible then omental biopsy should be done as a minimal surgical staging procedure.[13,15]

Some studies are done to prove that peritoneal biopsy is sole procedure responsible for upstaging in early stage ovarian cancer. However they all are unclear for the same. In our study, only 33 cases underwent random peritoneal biopsies. Out of 33 cases 4 (12%) has positive random peritoneal biopsies in our data. According to Shroff et al microscopic spread to peritoneal tissue is uncommon (6/122, 5%).[13] Furthermore, when a tumour is substantially restricted to the ovaries, Powless et al conclude that peritoneal biopsies provide little more diagnostic value than a comprehensive examination of all peritoneal surfaces.[15] Only one of 118 individuals with no gross/ suspicious disease beyond the ovary was upstaged to stage 2 disease based on the results of a random biopsy in the result of Powless et al .[15]

According to Ayhan et al random peritoneal biopsy of upper abdomen structures and appendicectomy led to upstaging in 12 (7%) of 169 cases.[16] However in our institute we don't routinely do appendicectomy in all cases except mucinous variety of cancer. Characteristics of upstaged patients are described in Table 3.

"Ayhan et al discovered that stage, the presence of ascites, and an elevated CA-125 level were all associated with the patients' upstaging".[16] A study by Helewa et al found that "upstaging was correlated with the endometroid histology".[19] However, serous is the most often observed histological finding among the 14 patients upstaged by the results of a random biopsies and omentectomy in our study; but this finding is not statistically significant with our small number of cases.

Regardless of these constraints, peritoneal biopsies of apparently normal appearing tissue can play a role in upstaging ovarian cancer patients, eventually leading to adjuvant treatment like chemotherapy. This emphasises the significance of examining all peritoneal surfaces thoroughly. This finding is especially important as the use of minimally invasive surgery for gynaecologic cancers is becoming more popular, obviating the need for palpation and emphasising the importance of thorough visual and histologic examination. There is no data on the potential increased benefits of more random biopsies, so more research is needed in this area.

Other future directions include examining the behaviour of cancers that spread to the peritoneum in an occult manner to see if their prognosis differs from those who are upstaged by gross disease.

Conclusion

In our study, omentectomy is significantly upstaging the early stage of ovarian cancer. Hence omentectomy must be a part of staging laparotomy in early stage epithelial ovarian cancer. Due to few positive outcomes in biopsies, peritoneal biopsies do not appear to be beneficial for early stage epithelial ovarian cancer. To verify and build on our findings, more study with a bigger sample size is required.[12]

References:

1. Hyuna S, Jacques F, Rebecca LS et al: Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. A Cancer Journal of Clinician 2021; 71:209-249
2. McLemore MR, Miaskowski C, Aouizerat BE, Chen LM, Dodd MJ: Epidemiological and genetic factors associated with ovarian cancer. Cancer Nurse. 2009; 32:281-288
3. Cho KR, Shih LM. Ovarian cancer: Annual Review of Pathology: Mechanism of disease 2009; 4:287–313
4. Berek JS, Berek DL: Berek & Novak's Gynecology 16th edition. Berek JS, editor. Philadelphia: Wolters Kluwer: 2020; 7:2716
5. Ng JS, Low JJ, Ilancheran A: Epithelial ovarian cancer. Best Practice and Research Clinical Obstetrics and Gynecology 2012; 26:337-345
6. Kleppe M, Wang T, Van Gorp T, Slangen BFM, Kruse AJ, Kruitwagen RFPM: Lymph node metastasis in stages I and II ovarian cancer: a review. Gynecology Oncology 2011; 123:610-614
7. Lengyel E: Ovarian cancer development and metastasis. The American Journal of Pathology 2010; 177:1053-1064
8. Semaan AY, Abdallah RT, MacKoul PJ: The role of laparoscopy in the treatment of early ovarian carcinoma. Europian Journal of Obstetrics and Gynecology Reproductive Biology 2008; 139:121-126
9. Köbel M, Huntsman D: Molecular pathology of ovarian carcinomas. Surgical Pathology Clinics 2011; 4:275-296
10. Le O: Patterns of peritoneal spread of tumor in the abdomen and pelvis. World Journal of Radiology 2013; 5:106
11. Berek JS, Bast RC Jr: Epithelial ovarian cancer. In: Kufe DW, Pollock REP, Weichselbaum RR, Bast RCJJ, Gansler TSG, Holland JFH et al: editors. Holland-Frei Cancer Medicine 6th edition. Hamilton:2003
12. Purbadi S, Anggraeni TD, Vitria A: Early stage epithelial ovarian cancer metastasis through peritoneal fluid circulation. Journal of Ovarian Research 2021; 14:44
13. Shroff R, Brooks RA, Zighelboim I, Powell MA, Thaker PH, Mutch DG et al: The utility of peritoneal biopsy and omentectomy in the upstaging of apparent early ovarian cancer. International Journal of Gynaecology Cancer 2011; 21:1208-1212
14. Berek JS, Hacker NF: Ovarian cancer. In: Berek and Hacker's Gynecologic oncology 7th edition. Philadelphia: 2021: 1102
15. Powless CA, Bakkum-Gamez JN, Aletti GD, Cliby WA: Random peritoneal biopsies have limited value in staging of apparent early stage epithelial ovarian cancer after thorough exploration. Gynecology Oncology 2009; 115:86-89
16. Ayhan A, Gultekin M, Celik NY, Dursun P, Taskiran C, Aksan G et al: Occult metastasis in early ovarian cancers: risk factors and associated prognosis. American Journal of Obstetrics and Gynecology 2007; 196:81e1-e6
17. Garcia- Soto AE, T Boren, Wingo SN, Heffernen T, Miller DS: Is comprehensive surgical staging needed for thorough evaluation of early stage ovarian carcinoma? American Journal of Obstetrics and Gynecology 2012; 206:242e1-e5
18. Arie AB, McNally L, Kapp DS, Teng NN: The omentum and omentectomy in epithelial ovarian cancer: a reappraisal: Part II—the role of omentectomy in the staging and treatment of apparent early stage epithelial ovarian cancer. Gynecology Oncology 2013; 131:784-790
19. Helewa ME, Krepart GV, Lotocki R: Staging laparotomy in early epithelial ovarian carcinoma. American Journal of Obstetrics and Gynecology 1986; 154:282-286