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Retrospective Observational Study of comprehensive Staging Surgery in Presumed Early Ovarian Cancer: 5 Years' Experience of Tertiary Cancer Centre of India

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ABSTRACT

The LION'S trial found that patients with advanced ovarian cancer who had therapeutic lymphadenectomy did not gain any advantages. This study sought to determine whether or whether individuals with early-stage ovarian cancer require more involved surgical procedures. This study is a retrospective observational analysis of 106 women diagnosed with ovarian cancer (FIGO Stage I) and treated at the Tata Medical Center in Kolkata with pelvic and para-aortic lymphadenectomy and complete omentectomy between September 2014 and September 2019. The study will be conducted between September 2014 and September 2019. According to the GOG criteria, a pelvic lymphadenectomy with removal of a minimum of ≥8 lymph nodes was considered adequate. 39% of patients went through main surgery, while 61% went through completion surgery (23 patients had their hysterectomy completed and 42 patients had their cystectomy completed). High grade serous tissue (n = 30), clear cell tissue (n = 22), low grade serous tissue (n = 5), endometrioid tissue (n = 29), mucinous tissue (n = 10), undifferentiated tissue (n = 3), sero mucinous tissue (n = 5) and poorly differentiated tissue (n = 3). In 77% of pelvic cases and 50% of para-aortic instances, the lymphadenectomy was effective in removing cancerous lymph nodes. Lymph nodes that had metastasized were located in the pelvis in 6% of individuals and the paraaortic region in 4%. There was a 6% incidence of omental metastases among the patients. In 2% of the patients, metastatic disease was discovered in the para-aortic nodes as well as the pelvic area. Out of the thirty patients diagnosed with HGSC, three were found to have metastases to the omentum, three to the pelvic nodes and one to the para-aortic node, as determined by the results of the subgroup analysis. Cancer had not progressed to the pelvic or para-aortic nodes in any of the twenty-two CCC patients and only two patients had cancer in their omentums. There was evidence of metastasis to the pelvic nodes in just one of the 29 patients diagnosed with endometrial cancer and there was no evidence of metastasis to the omentum or para-aortic nodes in any of the patients. One of the five patients with LGSC went on to develop metastases in the pelvic node, while another patient had metastases in the para-aortic node, despite the fact that there was no deposit in the omentum. In 14% of patients had their cancer stage raised from I to III after further testing. There is a correlation between having a pelvic lymphadenectomy and improved survival. Omentectomy and paraaortic lymphadenectomy did not improve the patient's chances of survival. It is past time that we reevaluate the practice of doing thorough staging surgery on presumptive early cases of ovarian cancer.

OPEN ACCESS

Key Words

HGSC-high grade serous carcinoma, CCC-Clear cell carcinoma, EC-endometrioid carcinoma, MC-mucinous carcinoma, LGSC-Low grade carcinoma, UC-undifferentiated carcinoma, PDC-poorly differentiated carcinoma, SMC-seromucinous carcinoma

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INTRODUCTION

Patients who have been diagnosed with ovarian cancer often get both surgical treatment and adjuvant chemotherapy that is based on platinum[1]. In addition, the patient's life expectancy is directly proportional to the level of success achieved during the surgery[2,3]. In patients who have advanced epithelial ovarian cancer, conducting maximum debulking to eliminate all macroscopic disease is the greatest predictor of survival. This is because maximal debulking removes as much of the disease as possible. However, surgical staging is essential at the apparent early stage of the illness in order to detect concealed metastases, which is necessary for determining adjuvant therapy and improving survival[1]. The usual surgical treatment for ovarian cancer continues to consist of removal of the uterus and both ovaries as well as comprehensive staging procedures[1]. Comprehensive staging surgery provides the potential to detect women who have more advanced stages of ovarian cancer[4]. Ovarian cancer with an apparent early stage has occult lymph node metastases in 5-20% of cases. When lymphatic and omental metastases are discovered during complete staging surgery[1,5], adjuvant treatment is required to treat the condition. Previous research has shown that patients with early-stage ovarian cancer who have lymphadenectomy had a lower risk of passing away as a result of the illness[6,7]. Patients who had advanced stages of ovarian cancer were not assisted by having complete lymphadenectomy performed, according to the results of the LION'S experiment. The major goal of this study was to examine the prevalence of omental, pelvic and paraaortic lymph node metastases in early-stage ovarian cancer. One of the secondary goals of the trial was to determine whether or not complete surgical staging improved overall survival for individuals with early-stage ovarian cancer.

MATERIAL AND METHODS

This study looks back at data collected via observation at Kolkata's Tata Medical Centre. Patients who meet the criteria will have had a pelvic and para-aortic lymphadenectomy as well as an omentectomy for radiologically suspected FIGO stage I ovarian cancer between September 2014 and September 2019, making them eligible for the study. Participants are required to have had these operations performed within the dates that have been indicated. The possibility of having cancer of the ovary that is aggressive and starts in the epithelium of the ovary was examined. Women who did not meet the exclusion criteria were not included in the research. These women either had stage II-IV illness, a non-epithelial histological type, inadequate data for pelvic and paraaortic lymphadenectomy and omentectomy, or borderline ovarian tumors. Additionally, there were insufficient data for pelvic and paraaortic lymphadenectomy and omentectomy. As previously indicated[8-10], the histology of ovarian cancer was defined using the World Health Organization (WHO) histological classification codes and the international classification of diseases, Third revision, site-specific terms for cancer. Data regarding patient characteristics (age at diagnosis, MI, prior history of treatment for ovarian cancer), tumor characteristics (cancer stage, histology types), lymphadenectomy and omentectomy, survival (alive/dead, disease free survival in months, date of last follow up) and recurrence (number of recurrences, sites of recurrences) were all recorded for each case that qualified for the study. Lymph nodes (pelvic and/or para-aortic) were counted and the frequency with which lymphadenectomy was performed was recorded. The length of time between a patient's ovarian cancer diagnosis and their death from the disease was considered their "Overall survival." Women who had died from any other reason or who were still living as of the most recent follow-up were omitted from the study since they were not included in the data set. The time period that was used to determine relapse-free survival was from the day when treatment was stopped to the date of recurrence or death. An acceptable pelvic lymphadenectomy, as outlined in the GOG Surgical Procedure Manual[11], requires the removal of a minimum of 8 lymph nodes in order to be considered successful. In this inquiry, the benchmark for sufficiency was determined to be the lymph node count level that was employed. The final model for this multivariate study took into account the features of the patient, the characteristics of the tumor and the results of the surgical procedure. As an indication of the degree of statistical significance, a hazard ratio (HR) that had been adjusted and a confidence interval (CI) that was 95% were reported. For each of the four histologic subtypes (mucinous, endometrioid, clear cell and serous), a sensitivity analysis was carried out to investigate the efficiency of proper lymphadenectomy and to estimate the likelihood of survival after the procedure. This conclusion was reached on the basis of the hypothesis that various histological subtypes of ovarian cancer each have their own unique biology and outlook[12-16]. All hypotheses with two potential outcomes were tested statistically and results were considered to be statistically significant if the p-value was less than 0.05. IBM's Statistical Package for the Social Sciences (IBM SPSS) was used to compile the data for the research. What do you think the chances are of succeeding?

RESULTS

Following the application of criteria for participation, 106 patients met the requirements to be considered for the research. 41 out of 106 patients received primary surgery, while 65 out of 106 patients got completion surgery (23 patients had TAH BSO and 42 patients had cystectomy). High grade serous tissue (n = 30), clear cell tissue (n = 22), low grade serous tissue (n = 5), endometrioid tissue (n = 29), mucinous tissue (n = 10), undifferentiated tissue (n = 3), sero mucinous tissue (n = 5) and poorly differentiated tissue (n = 3).

Seventy secen percent of pelvic lymphadenectomy and 50% of para aortic lymphadenectomy were sufficient. Six percent of individuals were found to have metastatic pelvic lymph nodes. 4 percent of patients developed metastatic nodes in the para-aortic region. Six percent of patients developed metastases to the omentum. Two percent of patients had metastases in both the pelvic and paraaortic nodes. The subgroup analysis revealed that of the 30 patients diagnosed with HGSC, 3 had metastases to the omentum, 3 to the pelvic nodes and 1 to the paraaortic node. In four of the twenty-two CCC patients, the sole location of metastasis was in the omentum and neither the pelvic nor the paraaortic nodes were implicated. Only one patient out of the 29 people who were diagnosed with endometrial cancer had any evidence of metastasis to the pelvic nodes and none of the patients had any evidence of metastasis to the omentum or the para-aortic nodes. Although there was no deposit in the omentum, one of the five patients with LGSC went on to develop metastases in the pelvic node and another patient acquired metastases in the para-aortic node. Only one of the 10 patients diagnosed with metastatic colorectal cancer had metastasis to the omentum and none of the patients had metastasis to the pelvic or paraaortic nodes. All five patients with SMC had metastases to the pelvic and para-aortic nodes, however only one patient had metastasis to the omentum. In the only PDC patient with metastatic disease, only the pelvic and paraaortic nodes were affected. 96.23% (102) patients were alive at the end of study period. Mean time of survival is 54.730 months (95% CI is 51.52-57.94). There was a recurrence in 17 patients (16.04%). The 95% confidence interval for the mean period between recurrences is between 40.22 and 50.63 months (Fig. 1).

Using the kaplan-meyer curve and the log rank test, researchers determined that pelvic node metastasis significantly reduced overall survival compared to paraaortic node metastasis and omental metastasis. (56.698 months vs 33.600 months, p = 0.0096). No significant overall survival outcome of paraaortic (p = 0.6580) and omental (p = 0.6928) metastasis.

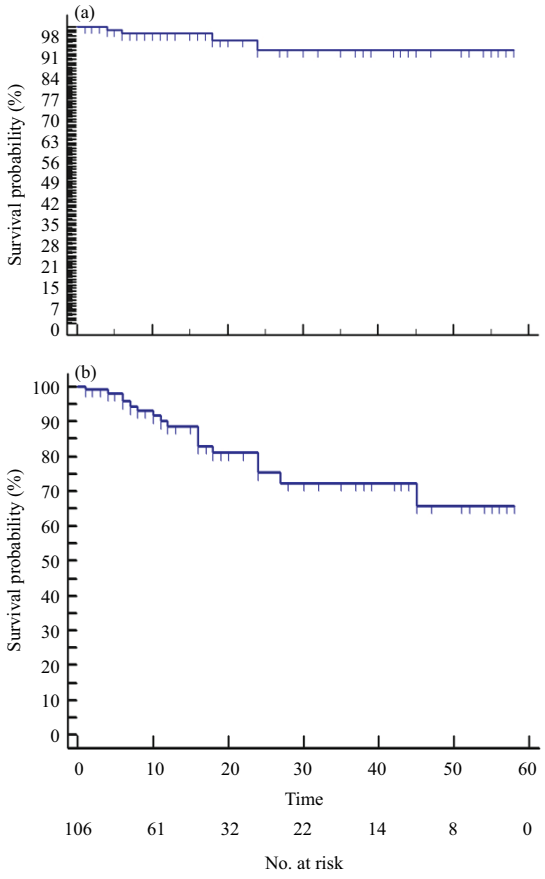

Fig. 1(a-b): Showing recurrence and risk ratio of the TMC individuals of the present study

Recurrence free survival is statistically significant in omentum negative group (46.697 vs 18.604 m, p = 0.0016) and pelvic node negative group (47.773 vs 26.714 m, p = 0.0327) but not in paraaortic node negative group (46.453 vs 23.333 m, p = 0.0884) (Table 1).

When overall survival was analyzed with pelvic, para-aortic lymph node status, omentum, histology and main and completion surgery, age and CA 125 value, pelvic node positive and age $\geq$50 were shown to be significantly associated with overall survival. Logistic regression was used to get this conclusion. Furthermore, there is no strong correlation between histology, primary or secondary surgery, age >50 years, or a CA 125 level >70 at the time of diagnosis and the presence of positive pelvic lymph nodes or omentum. (For pelvic node p = 0.0601, omentum p = 0.1923). Patients with any stage of clear cell, high-grade serous, undifferentiated, seromucinous, or poorly differentiated cancer received adjuvant therapy. Adjuvant chemotherapy was given from the tumor's IC onward throughout the rest of the histology. Only three patients out of 106, or 2.8%, who were upstaged from IA/IB to Stage III had adjuvant chemotherapy added to their treatment because they had lymph

Table 1: Different types of the nodal cancer with recurrence and death rate in the patients of the present study

Types	No.	Positive pelvic node	Positive para aortic node	Omental mets	Recurrence	Death	Mean recurrence time (months)	Mean survival time (months)
HGSC	30	3	1	3	6	2	33.960	42.368
EC	29	1	0	0	2	1	51.333	54.222
CCC	22	0	0	2	6	1	39.252	53.263
MC	10	0	0	1	1	0	49.556	55.000
Overall	106	7	4	6	17	4	45.425	54.730

Table 2: Characteristics of the patients' nodal tissue pathology of the present study

Variables	p-value	HR	95% CI of HR
Age ≥50 years	0.0176	35.3403	1.8641 to 669.9770
CA 125 >70	0.3864	0.2625	0.0127 to 5.4154
Pelvic node positivity	0.0434	101.7909	1.1465 to 9037.5903
Omentum positivity	0.9771	0.0001	9.1176E-292 to 4.2891E+282
Para aortic node positivity	0.9789	0.0005	5.9464E-246 to 49.6383E+237
Histology	0.1875	0.2394	0.0286 to 2.0060
Primary vs completion surgery	0.7723	1.5446	0.0813 to 29.3572

node or omentum positivity. If these patients had not been positive for lymph nodes or omentum, they would have been retained under follow up. The pelvis (number seven) was the most likely location for a cancer to return after treatment. Eight patients had second-line chemotherapy as part of their recurrence care, while another five received secondary cytoreduction plus second-line chemotherapy.

DISCUSSIONS

In the earlier stages of ovarian cancer, such as stages IA and IB, except for the serous kind, many women choose not to undergo chemotherapy treatment. Some women have fewer cycles of chemotherapy than others, even if they have more advanced stages of the cancer. Therefore, establishing the precise stage of the disease is helpful for customizing adjuvant treatment. When full staging surgery is performed, it is easier to diagnose advanced stage illness because it improves the ability to detect concealed metastases by sufficient pelvic and para-aortic lymphadenectomy and omentectomy[1,4]. This makes advanced stage disease identification more likely.

When a higher nodal cut-point was used, there was a little reduction in the survival benefit of sufficient lymphadenectomy (cause-specific mortality: With 8-12 nodes, there is a 25% reduction whereas for >22 nodes, there is a 15% reduction). This suggests that in the early stages of ovarian cancer, an excision of 8-12 nodes is adequate for detecting a single nodal metastasis. These findings are in line with those of a more recent cohort research that investigated the impact of removing ≥10 lymph nodes from individuals who were diagnosed with early-stage ovarian cancer[17].

Lymphadenectomy was shown to be sufficient and favorable to survival for serous, endometrioid and clear cell malignancies[18]. This was the case for each histologic subtype of the malignancy. On the other hand, there was no correlation between the removal of lymph nodes in a mucinous type tumor and an improvement in the patient's chance of survival[18]. During the course of our study, a somewhat more advanced stage was designated for each of the fourteen patients who participated. Adjuvant chemotherapy is provided to patients who are being treated at our clinic for high-grade serous and clear cell ovarian tumors, regardless of the stage of the illness. Only 4% of 52 patients with low-grade serous, endometrioid, mucoid, or seromucinous carcinoma were reclassified from stage I to stage III and so received adjuvant therapy. This represents an eight percent upstage rate. Lymphadenectomy is associated with a high rate of severe morbidity (17.5%) but only a 2.5% death rate. Completion surgery has a 50% higher risk of complications than initial surgery. Therefore, out of 103 patients, the treatment plan was revised to only apply to three patients by performing complete staging surgery and the remaining 102 patients were subjected to unnecessary additional surgical morbidity as a result. The obvious next question that has to be asked is whether or not all patients require extensive staging surgery or whether it can be personalized. The research was conducted out by a single institution with a small number of participants and there was no effort made to analyze the individuals' overall quality of life. Both of these aspects are weaknesses in the study[19-22].

CONCLUSION

Fourteen percent of patients had their cancer stage raised from I to III after further testing. There is a correlation between having a pelvic lymphadenectomy and improved survival. Omentectomy and paraaortic lymphadenectomy did not improve the patient's chances of survival. Ovarian cancer patients who are first identified with the disease while it is in its early stages need a thorough examination to determine whether or not they should have total staging surgery. This makes it possible to carry out prospective randomized trials and then perform an analysis on the data obtained from those trials.

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