

Therapeutic Significance of Comprehensive Lymphadenectomy in Early-stage Clear Cell Carcinoma of Ovary

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Abstract

Aim: This study aims to study the therapeutic significance of full lymphadenectomy in early-stage ovarian clear cell carcinoma.

Methods: This prospective study was conducted in the patients with early-stage epithelial cell carcinoma. The following procedures were performed: Bilateral salpingo-oophorectomy and hysterectomy (if not previously performed), washing, random multiple peritoneal biopsies, omentectomy, and systematic pelvic and para-aortic lymphadenectomy.

Results: A total of 96 of 107 women with epithelial cell carcinoma were suitable for analysis. Endometrioid (35.5%), serous (22.4%), and clear cell (7.5%) cancers represented in the histological types. 12.5% rate of lymph node metastases in apparent epithelial cell carcinoma after lymph node assessment, no cases reported in clear cell carcinoma.

Conclusion: The present results suggest that some patients with selected early-stage clear cell carcinoma may benefit from full lymphadenectomy.

Key words: Clear cell adenocarcinoma, Lymph node excision, Lymphatic metastasis, Ovarian

INTRODUCTION

Epithelial ovarian cancer is the most lethal gynecologic malignancy. Effective screening strategies are lacking and most women are diagnosed with advanced stage disease. Clear cell carcinomas of the ovary (CCO) have distinct clinical and histopathological characteristics and poor treatment outcomes as compared to other epithelial cancers of the ovary.^[1] CCO has been defined by the World Health Organization as an ovarian carcinoma characterized by clear cells growing in solid/tubular or glandular pattern.^[2] Women with an isolated pelvic mass are often completely asymptomatic until the mass itself produces distension or pelvic pressure. Complete surgical

staging will “upstage” a patient with an isolated ovarian mass in up to 30% of patients due to occult disease.^[3] Surgical staging for Stage I disease may involve incidental finding postoperatively or through intraoperative frozen pathologic confirmation after intact mass excision. If the lesion is determined intraoperatively, comprehensive staging is recommended through laparotomy, with peritoneal washings, complete hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy, and examination/sampling of peritoneal surfaces of the diaphragm, paracolic gutters, and pelvis.^[4] Post-operative discovery should involve a gynecologic oncology consultation and decision tree involving histology, grade, potential of residual disease, and fertility potential. Conservative surgery for younger patients with the low-grade disease is certainly indicated, including preservation of the remaining normal ovary and the uterus, but absolute ascertainment of the grade of disease should be determined if possible. High-grade tumors in younger patients usually require complete surgical staging and adjuvant therapy but must be considered in context

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with the patient's circumstances and risk assessment.¹⁵⁻⁷¹ Treatment with chemotherapy will depend on the presence of complete surgical staging and the grade of disease.

Aim

This study aims to study the therapeutic significance of full lymphadenectomy in early-stage ovarian clear cell carcinoma.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Surgical Oncology, Regional Cancer Centre at Government Coimbatore Medical College and Hospital on patients with early-stage epithelial cell carcinoma. All patients provided written informed consent. Patients included in the analysis were those who received total surgery with the aim of eradicating the primary malignancy. Exclusion criteria were extrapelvic metastatic disease, tumors of low malignant potential, and previous retroperitoneal surgery. The following procedures were performed: Bilateral salpingo-oophorectomy and hysterectomy (if not previously performed), washing, random multiple peritoneal biopsies, omentectomy, and systematic pelvic and para-aortic lymphadenectomy. The para-aortic systematic lymphadenectomy was performed after opening the retroperitoneum as far as the Treitz ligament and along the paracolic gutters. It included the following steps: The lymphofatty tissue located between the psoas muscles was removed laterally and the inferior vena cava medially as far as the right renal vein (the lymph nodes from this tissue were named paracaval lymph nodes); the removal of the lymph nodes located between the aorta and the cava, from the aortocaval bifurcation as far as the left renal vein (these were named interaortocaval lymph nodes); and the removal of the lymph nodes located between the aorta and left psoas muscle from aortocaval bifurcation as far as the left renal vein (these were named para-aortic lymph nodes). The pelvic systematic lymphadenectomy included the removal of the lymphofatty tissue located above the external iliac vessels between the iliac bifurcation, the inferior epigastric vessels, and psoas muscle laterally; these lymph nodes were named external iliac lymph nodes. The dissection continued with the removal of the lymph nodes located below the external iliac vessel and above the obturator nerve, between the iliac bifurcation, the psoas muscle laterally, the obturator muscle caudally, and the virtual plane passing through the umbilical artery and bladder medially; these lymph nodes were named obturator lymph nodes. The lymphadenectomy was completed with the removal of the lymph nodes located above and lateral to the common iliac lymph nodes between the aortocaval bifurcation and the iliac bifurcation; these were named common

iliac lymph nodes. A laparoscopic conservative surgical approach consisted of unilateral salpingo-oophorectomy and complete staging and systematic bilateral pelvic and para-aortic lymphadenectomy. The uterus and one ovary were retained in patients under the age of 40 who strongly wished to retain their fertility. Demographic, clinical, surgical, and pathologic characteristics of the patients were assessed. Pathology information included tumor histology, grade, and stage at diagnosis, number of regional lymph nodes examined, and number of metastatic lymph nodes removed, as well as documented extension away from the primary site.

RESULTS

A total of 96 of 107 women with early-stage epithelial cell carcinoma were suitable for analysis. 11 patients were excluded from our study and did not undergo lymph node evaluation: Eight patients with mucinous IA cancer, one elderly patient with concomitant morbidities, and two who had previously undergone retroperitoneal surgery. Endometrioid (35.5%), serous (22.4%), and clear cell (7.5%) cancers represented in the histological types. In 44.6% of cases, the tumor was poorly differentiated. Node metastases were found in 12 patients (12.5%). The pattern of positive nodes was as follows: 3 (25%) of 12 from the para-aortic and pelvic areas, 1 (8.3%) of 12 only from the pelvic area, and 8 (66.6%) of 12 from only the para-aortic area. 11 (91.6%) of 12 patients had lymph node metastases in the para-aortic region [Tables 1 and 2].

The disease of 14 patients (14.5%) was upstaged, 13 for node metastases and 1 for pelvic peritoneal involvement. There were two major intraoperative complications: Vascular injury and obturator nerve injury. Both were managed intraoperatively. In the early post-operative period, one patient experienced bleeding, one patient experienced deep venous thrombosis, and two patients experienced lymphorrhea. One case of vaginal cuff dehiscence was reported. Late post-operative complications were eight lymphocyst formation and one post-operative abdominal hernia. Overall, post-operative lymphadenectomy-related complications (lymphocysts and lymphorrhea) were observed in 14 patients (14.5%). There was no surgical mortality. Two patients developed lymphorrhea, which were subsequently treated with a hypolipidemic diet and drainage.

DISCUSSION

The detection of metastatic disease in the lymph nodes after complete surgical staging is prognostically significant. In these cases, adjuvant therapies, as for

Table 1: Clinical and pathologic characteristics

Characteristics	Value
Age	
Median	50
Menopausal status	
Pre	49
Post	58
Histological type	
Mucinous	14
Serous	24
Endometrioid	38
Clear cell	8
Mixed histology	15
Undifferentiated	8
Grade	
1	24
2	33
3	50

Table 2: Patients with node metastases by histological type

Histological type	Value
Mucinous	0
Serous	6
Endometrioid	3
Clear cell	0
Mixed histology	1
Undifferentiated	2

advanced disease, are necessary. Lymphadenectomy not only reveals the real spread of apparent epithelial cell carcinoma but is also a means of removing any retroperitoneal metastatic disease. We found a 12.5% rate of lymph node metastases in apparent epithelial cell carcinoma after lymph node assessment, and the disease of 14 (14.5%) of 96 patients was upstaged after complete staging. There are many prognostic factors identifiable before or during surgery that can predict the spread of retroperitoneal disease. Lymph node evaluation should always be integrated in complete staging of epithelial cell carcinoma because in patients with lymph node metastases, the systematic lymphadenectomy has a prognostic and potentially therapeutic role. In addition, an upstaging warrants adjuvant treatment, while a complete surgical staging could avoid further medical treatment, according to the ICON-ACTION trial.^[8,9] In this prospective study, we found a node-positive rate of 12.5%. The distribution of positive nodes was as follows: 25% from the para-aortic and pelvic areas, 8.3% from the pelvic area alone, and 66.6% from only the para-aortic area. The node-positive rate in the para-aortic region was as high as 91.6%. Data from previous papers reported nodal involvement in 4–25% of patients with tumor apparently confined to the ovaries. When we evaluated only data from systematic lymph node dissection, the

mean rate of retroperitoneal metastases was 14%, ranging 12–26%.^[10-12] Data in literature report that serous adenocarcinoma is characterized by the highest incidence of node metastases. The serous histotype spreads in a third to a quarter of cases in the retroperitoneal space, while epithelial cell carcinoma mucinous tumors rarely spread to the lymph nodes.^[10-12] In the present study, clear cell and undifferentiated tumor, grouped in the category “other,” presented node metastases in 9.8% of cases. Data in literature reveal that endometrioid, clear cell, and undifferentiated tumors behave similarly.^[13] The histological subtype could not have been a significant and independent risk factor for node positivity because the number of patients with more aggressive histotypes (clear cell and undifferentiated) was not so representative.

CONCLUSION

A tailored approach, however, should always be kept in mind. On the basis of the present series and the data in literature, omitting a systematic lymphadenectomy can be considered for Grade I cancers and mucinous tumors regardless of grade.

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