Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Clinical, Radiological, Pathological Correlation of Nodal Status in Operable Epithelial Ovarian Cancer.

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Received: February 2018
Accepted: February 2018

ABSTRACT

Background: The aim of this prospective study is to correlate radiological and intraoperative nodal characterization with pathological examination of pelvic and para-aortic nodes in operable epithelial ovarian cancer. **Methods:** The patients with epithelial ovarian cancer who had surgical cytoreduction were included in the study. These patients were subjected to radiological assessment of the abdomen with CT scan for nodal deposits in the para-aortic and pelvic region and it was followed by surgical cytoreduction. Intraoperatively, the nodes were palpated before, and after nodal basin, facial planes were dissected. After nodal dissection, the lymph nodes were grossed and sampled clinically as significant and insignificant and placed in separate jars. These nodes were pathologically assessed. Pathologically positive nodes were correlated with radiological, intraoperative and grossing findings. **Results:** Of the 27 patients, mean age was 45.6±10.9 years. Nine patients underwent upfront surgery, 18 patients underwent interval cytoreduction. A significant correlation was obtained (P Value <0.001) with grossing after surgery with the final histopathological report. The probable chance of identifying significant lymph nodes obtained in final pathological report from grossing after surgery in para-aortic nodes, right pelvic nodes, left pelvic nodes, right common iliac nodes and left common iliac nodes were 55%, 50%, 67.7%, 81.25% and 61.53% were positive for deposits and for insignificant lymph nodes obtained in final pathological report from grossing after surgery were 83.3%, 86.3%, 89.1%, 79% and 92% respectively were negative for deposits. **Conclusion:** Grossing after surgical dissection of the lymph nodes best correlates with final histopathology. CT scan findings for lymph nodal status in epithelial ovarian cancer does not correlate with final pathology.

Keywords: Epithelial Ovarian Cancer, Pelvic and Para aortic lymph node dissection.

INTRODUCTION

Ovarian cancer remains one of the major cause of cancer-related death in females.[1,2] Around 60% of the patients present with metastasis beyond the pelvis at the time of the diagnosis.[3] The disease spreads to the lymph vessels that accompany the ovarian artery and vein in the infundibulopelvic ligament and goes para-aortic and para caval nodes below the level of renal hilum. Some lymphatics follows uterine vessels in broad ligament towards uterine artery and vein and follows to iliac vessels and goes to pelvic lymph nodes.[4-7] The incidence of positive para-aortic nodes in Stage I disease is 18.2 %, 20% in Stage II, 41.9% in Stage III, and 66.7% in Stage IV. The incidence of pelvic nodal metastasis is 9.1% in Stage I, 10% in Stage II, 12.5% in Stage III and 33.3% in Stage IV.[8] Nearly 10-20% of normal sized locoregional nodes will contain tumor deposits, and 30% of enlarged nodes will demonstrate only inflammatory reaction.[9] The designation of stage III A1 is based on the spread to retroperitoneal lymph nodes without intraperitoneal dissemination. The survival of these patients is better than that of patients with intraperitoneal dissemination. Nodal metastasis without peritoneal metastasis is relatively uncommon (about 9% of cases).[10-15] Most of these patients have positive para-aortic nodes.[13-17] The nodal status of the ovarian cancer is important for prognosis. Several studies have reported series on incidence and distribution of para-aortic lymph node metastasis in early ovarian cancer, but only a few studies have attempted to evaluate the para-aortic nodal involvement above inferior mesenteric artery.[18]

The lymph nodes can be evaluated preoperatively with imaging techniques such as CT scan. The imaging criteria used to assess lymph node metastasis are based on nodal size with abnormal being >1cm. Malignant nodes demonstrate irregular borders due to the extra capsular extension of disease.[14] The CT and MR imaging are shown to

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perform well in assessing adenopathy. However because there may be false positive causes of enlarged nodes from benign disease, the sensitivity, and specificity in detecting lymph node metastasis of CT scan is 42% and 95%, MRI is 54.7% and 88.3%, and PET CT is 73.2% and 96.7% respectively.[14] We had correlated the nodal status of epithelial ovarian cancer with CT scan findings, intraoperative nodal status findings, grossing after surgery with final histopathology report.

Aim

To correlate the radiological, clinical (intra operative nodal characteristics), pathological correlation of pelvic and para aortic nodes in the patients with epithelial ovarian cancer who undergone staging.

MATERIALS AND METHODS

This prospective study was conducted in Centre For Oncology, GRH, Kilpauk Medical College, Chennai. Patients with early malignant ovarian tumor and advanced tumor post-neoadjuvant chemotherapy were included in this study. Poor performance status, bulky intraabdominal disease assessed by CT and stage IV disease were excluded from the study. Imaging with CT scan of abdomen and pelvis was done [Figure 1]. CT features of malignant nodes were lymph nodes that measured more than 1 cm in short axis with irregular borders were recorded. All patients were surgically staged according to FIGO standard surgical procedures [Figure 2]. Primary or interval cytoreduction was done. Pelvic and para-aortic nodes were assessed intraoperatively [Figure 3]. Inspection and palpation of nodes in the pelvic and para-aortic region were done before and after the opening of retroperitoneum and classified as significant and insignificant nodes. Nodes palpable (more than 1 cm, hard, rounded) were recorded. All the patients underwent pelvic and para-aortic lymph nodal dissection [Figure 4]. All the lymph nodes in the corresponding areas were grossed into significant and insignificant lymph nodes depending upon size, consistency, and perinodal spread. The lymph nodes were sent for histopathological examination and correlated with the radiological and clinical parameters to get the reliability of the above modalities in predicting malignant deposits. We had divided Boundaries for lymph node dissection into three groups as follows:

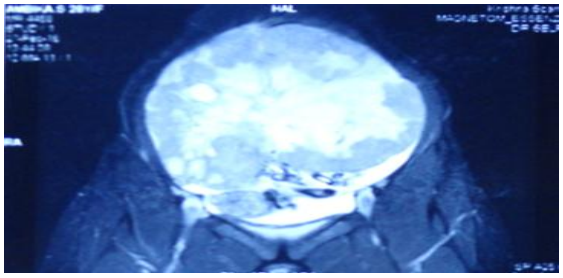

Figure 1: Imaging With CT Scan Of Abdomen And Pelvis

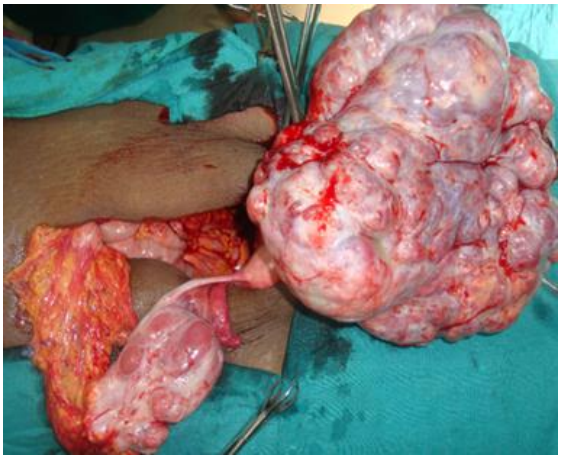

Figure 2: Intra Operative Findings

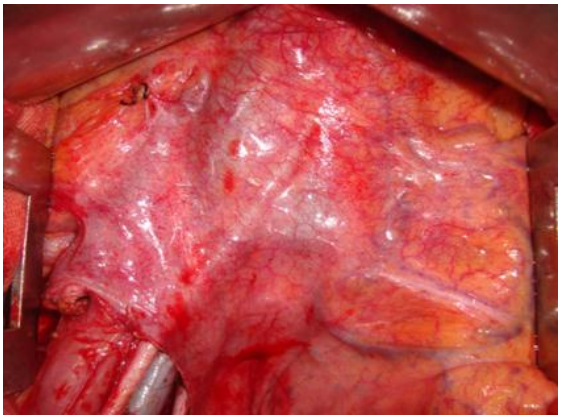

Figure 3: Before Opening Of Retroperitoneum Of Nodal Basin (Para Aortic Area)

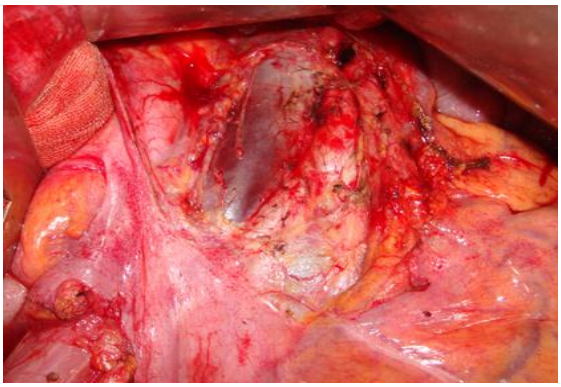

Figure 4: After Opening of Retroperitoneum Of Nodal Basin (Para Aortic Area).

Para Aortic Lymph node dissection

Superiorly renal vein, laterally ureters, caudally bifurcation of aorta.

Common Iliac Lymph Nodes

Extends from bifurcation of aorta to bifurcation of common iliac artery. Laterally by psoas muscle, medially by common iliac artery.

Pelvic Lymph nodes

Extends from bifurcation of common iliac artery to the point where deep circumflex iliac vein crosses

over external iliac artery. Lateral boundaries were psoas muscle and genitofemoral nerve. Medial boundaries were ureter and superior vesical artery.
All the lymph nodes in the corresponding areas were grossed by surgeon within 1 hour in to significant and insignificant lymph nodes. These lymph nodes were sent in separate jars to pathology department and histopathology was obtained.

Data Collection

Clinical, radiological and pathological parameters were recorded which includes patients age, stage, histological type and anatomic distribution of metastatic lymph nodes.

Statistical Analysis

All the data were tabulated and analysed by the SPSS package version 12. The level of significance was set as 0.05. Categorical variables were analyzed with Chi square test and continuous variable were analyzed with one way ANOVA and correlation done between two parameters.

RESULTS

Of the 27 patients, mean age was 45.6±10.9 years. Most commonly presented with mass and pain abdomen and 22 patients (81.5%) presented with stage IIIC. About 9 patients underwent upfront surgery, 18 patients underwent interval cytoreduction. Most common histopathology noted was serous cystadenocarcinoma (77.8%) [Table 1].
When comparing the variables with final histopathology report in the para-aortic nodal area, there was a high chance of getting nodal metastasis obtained in lymph nodes with surgical exposure of nodal basin (32.2%) and grossing done after surgery (32.1%). In remaining pelvic nodal areas, there is a high chance of getting nodal metastasis in grossing after surgery [Table 2].
For para-aortic lymph nodal metastasis, grossing after surgery correlates with final pathology (P-value 0.001) followed by radiological findings, palpation before and after exposure of nodal basin. For right common iliac lymph nodes, grossing after surgery (P-value 0.001) correlates highly with final pathology, followed by palpation without exposure of nodal basin. For left common iliac lymph nodes, grossing after surgery (P-value 0.001) highly correlates with the final pathology. For right pelvic lymph nodes, grossing after surgery (P-value 0.001) followed by palpation with exposure of nodal basin correlates with final pathology. For left pelvic lymph nodes, grossing after surgery (P-value 0.001) followed by palpation without exposure of nodal basin correlates with the final pathology [Table 3].
A significant correlation was obtained (P Value <0.001) with grossing after surgery with the final histopathological report. Patients had no significant correlation with radiological findings with the final histopathological report when compared with grossing after surgery.

Para-aortic lymph nodes

Among the 27 patients, radiologically an average 6 lymph nodes were found to be significant. Per-operatively, before the opening of the retroperitoneum, an average 8 lymph nodes were identified. After exploring the nodal basin, an average 10 lymph nodes were found. After grossing, there were 36 (33.3%) significant and 72 (66.7%) insignificant nodes identified. Pathologically among the significant lymph nodes, 20 had metastasis, and among insignificant lymph nodes, 12 had metastasis. The chance of identifying significant lymph nodes obtained in a final pathological report from grossing after surgery is 55%. The chance of identifying insignificant lymph nodes obtained in the final pathological report from grossing after surgery is 83.3%.

Pelvic lymph nodes-Right

Among the 27 patients, radiologically no lymph nodes were found. Per-operatively before the opening of retroperitoneum an average 5 lymph nodes were identified. After exploring the nodal basin, an average 9 lymph nodes were found. After grossing, there were 18 (14.6%) significant and 105 (85.4%) insignificant nodes identified. Pathologically among the significant lymph nodes, 9 had metastasis, and among insignificant lymph nodes, 14 had metastasis. The chance of identifying significant lymph nodes obtained in the final pathological report from grossing after surgery is 50%. The chance of identifying insignificant lymph nodes obtained in the final pathological report from grossing after surgery is 86.3%.

Pelvic lymph nodes-Left

Among the 27 patients, radiologically no lymph nodes were found. Per-operatively, before the opening of retroperitoneum, an average 5 lymph nodes were identified. After exploring the nodal basin, an average 9 lymph nodes were found. After grossing, there were 31 (23.5%) significant and 101 (76.5%) insignificant nodes identified. Pathologically among the significant lymph nodes, 21 had metastasis, and among insignificant lymph nodes, 11 had metastasis. The chance of identifying significant lymph nodes obtained in the final pathological report from grossing after surgery is 67.7%. The chance of identifying insignificant lymph nodes obtained in the final pathological report from grossing after surgery is 89.1%.

Common iliac lymph nodes-Right

Among the 27 patients, radiologically no lymph nodes were found. Per-operatively, before the opening of retroperitoneum, an average 3 lymph nodes were identified. After exploring the nodal basin, an average 5 lymph nodes were found. After grossing, there were 16 (45.7%) significant and 19

Table 1: Distribution Of Patient's Characteristics

Patient characteristics		Number of Cases	Percentage
Age	30 – 40 years	7	25.90%
	41 – 50 years	10	37.10%
	51 – 50 years	7	25.90%
	61 – 70 years	3	11.10%
Surgery	Interval, Cytoreduction	18	66.70%
	Upfront Surgery	9	33.30%
Histology	Serous cystadenocarcinoma	21	77.80%
	Mucinous cystadenocarcinoma	6	22.20%
Stage	IA	4	14.80%
	IIIC	22	81.50%
	IVA	1	3.70%

Common iliac lymph nodes-Left

(54.3%) insignificant nodes identified. Pathologically among the significant lymph nodes, 13 had metastasis, and among insignificant lymph nodes, 4 had metastasis. The chance of identifying significant lymph nodes obtained in the final pathological report from grossing after surgery is 81.25%. The chance of identifying insignificant lymph nodes obtained in the final pathological report from grossing after surgery is 79%. Among the 27 patients, radiologically no lymph nodes were found. Per-operatively, before the opening of retroperitoneum, an average 2 lymph nodes were identified. After exploring the nodal basin, an average 3 lymph nodes were found. After grossing, there were 13 (34.2%) significant and 25 (61.8%) insignificant nodes identified. Pathologically among the significant lymph nodes, 8 had metastasis, and among insignificant lymph nodes, 2 had metastasis. The chance of identifying significant lymph nodes obtained in the final pathological report from grossing after surgery is 61.53%. The chance of identifying insignificant lymph nodes obtained in the final pathological report from grossing after surgery is 92% [Table 4].

Table 2: Frequencies Between The Lymph Nodes Which Showed Positive Results In The Nodal Basins.

Findings	Positive Para Aortic Lymph Nodes% (number of patients)	Positive Right Common Iliac Nodes % (number of patients)	Positive Left Common Iliac Nodes% (number of patients)	Positive Right Pelvic Lymph Nodes % (number of patients)	Positive Left Pelvic Lymph Nodes % (number of patients)
Radiologic Findings	14.3% (4)	0%	0%	0%	0%
Palpation without exposure of nodal basin	17.9% (5)	3.6% (1)	0%	3.6% (1)	3.6% (1)
Palpation with exposure of nodal basin	32.2% (9)	7.1% (2)	0%	10.8% (3)	10.8% (3)
Grossing done after surgery (significant lymph nodes)	32.1% (9)	17.9% (5)	10.7% (3)	21.4% (6)	32.1% (9)
Final Pathology	21.4% (6)	10.7% (3)	10.7% (3)	32.1% (9)	28.6% (8)

Table 3: Correlation Of Final Pathology With Radiological Findings Without And With Exposure Of Nodal Basin, Grossing After Surgery.

		Mean (No. of cases) SD	P Value
Paraaortic Lymph Nodes	Final Pathology	3.29 ± 3.8	0.001
	Radiological findings	0.21 ± 0.6	
	Final Pathology	3.29 ± 3.8	0.002
	Palpation without exposure of nodal basin	0.43 ± 1.1	
	Final Pathology	3.29 ± 3.8	0.001
	Palpation after exposure of nodal basin	0.68 ± 1.2	
	Final Pathology	3.29 ± 3.8	0.001
	Grossing after Surgery	4.18 ± 5.1	
Right Common Iliac Lymph Nodes	Final Pathology	1.04 ± 2.1	Not Significant
	Radiological findings	0.00 ± 0.00	
	Final Pathology	1.04 ± 2.1	0.002
	Palpation without exposure of nodal basin	0.07 ± 0.4	
	Final Pathology	1.04 ± 2.1	0.088
	Palpation after exposure of nodal basin	0.14 ± 0.52	
	Final Pathology	1.04 ± 2.1	0.001
	Grossing after Surgery	1.11 ± 2.2	
Left Common Iliac Lymph Nodes	Final Pathology	0.5 ± 1.1	Not Significant
	Radiological findings	0.00 ± 0.00	
	Final Pathology	0.5 ± 1.1	Not Significant
	Palpation without exposure of nodal basin	0.00 ± 0.00	
	Final Pathology	0.5 ± 1.1	Not Significant
	Palpation after exposure of nodal basin	0.00 ± 0.00	
	Final Pathology	0.5 ± 1.1	0.001
	Grossing after Surgery	0.68 ± 1.2	
Right Pelvic Lymph Nodes	Final Pathology	4.25 ± 3.4	Not Significant
	Radiological findings	0.00 ± 0.00	
	Final Pathology	4.25 ± 3.4	0.39

	Palpation without exposure of nodal basin	0.18 ± 0.94	
	Final Pathology	4.25 ± 3.4	0.012
	Palpation after exposure of nodal basin	0.39 ± 1.2	
	Final Pathology	4.25 ± 3.4	0.001
	Grossing after Surgery	5 ± 4.4	
Left Pelvic Lymph Nodes	Final Pathology	5.46 ± 4.4	Not Significant
	Radiological findings	0.00 ± 0.00	
	Final Pathology	5.46 ± 4.4	0.001
	Palpation without exposure of nodal basin	0.18 ± 0.95	
	Final Pathology	5.46 ± 4.4	0.001
	Palpation after exposure of nodal basin	0.29 ± 1.0	
	Final Pathology	5.46 ± 4.4	0.001
	Grossing after Surgery	5.86 ± 4.6	

Table 4: Lymph Nodes Obtained

Number of lymph nodes found in	Pelvic Nodes		Para Aortic Lymph nodes	Common Iliac Lymph nodes	
	Right	Left		Right	Left
Radiological finding	0	0	6	0	0
Palpation without exposure of nodal basin	5	5	8	3	2
Palpation with exposure of nodal basin	9	9	10	5	3
Grossing after surgery(Significant lymph nodes)	18	31	36	16	13
Grossing after surgery(Insignificant lymph nodes)	105	101	72	19	25
Final pathology- number of positive nodes from significant lymph nodes	9	21	20	13	8
Final pathology- number of positive nodes from insignificant lymph nodes	14	11	12	4	2

DISCUSSION

Around 24.6% of apparent early ovarian cancer patients who underwent pelvic and paraaortic lymphadenectomy had lymph node metastasis on postoperative findings although preoperative CT performed in all patients did not reveal suspicious nodal metastasis.[3]

Potential pitfalls in nodal assessment on CT include:

a) Small bowel loops in proximity to retroperitoneum can mimic nodal disease.
b) Normal ovaries can mimic iliac nodal enlargement.
c) Blood vessels especially aberrant vessels can be mistaken for a lymph node especially on non-contrast enhanced CT; normal anatomic variants such as left-sided inferior vena cava or duplicated IVC may mimic nodal disease.
d) Prominent cistern chili can also simulate retrocrural nodal enlargement.
e) Peritoneal nodules can mimic mesenteric or pelvic lymph nodes.
f) Following surgery, lymphocoeles can mimic a low attenuation lymph node.[9]

In our study, final pathology obtained was highly correlated with the grossing after surgery which was statistically significant (P Value 0.001).

The role of lymphadenectomy as an integral part of surgical staging has been a subject of continuing debate, and its significance in ovarian cancer treatment is not yet completely established.[9] The presence of lymph node metastases can significantly alter the patient management, and therefore the accruable diagnosis of presence and extent of nodal metastasis can help optimize patient management.[9] Grossing of nodes done by the surgeon to decide significant nodes which were likely to be pathologically positive.

CONCLUSION

The accurate identification of malignant lymph node is a major challenge in diagnostic radiology. CT scan has limited ability to detect metastasis in lymph nodes. Grossing lymph nodes after dissection in nodal basin better correlate with the final histopathology.

Acknowledgement

I would like to thank Statistician Mr.Selvan Kuppusamy (Apollo Hospitals) and Research Associate Dr.J.Mohamed Ali (Dr.Agarwal's Healthcare Limited) for their support.

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How to cite this article: Subbiah S, Gopu G, Hussain SA, Singh RSB. Clinical, Radiological, Pathological Correlation of Nodal Status In Operable Epithelial Ovarian Cancer. Ann. Int. Med. Den. Res. 2018; 4(2):MC13-MC18.

Source of Support: Nil, **Conflict of Interest:** None declared