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Original Research Article

To Analyze the Patterns of Pelvic and Para-Aortic Lymph Node Involvement among Patients with Early Endometrial Cancers: An Observational Study

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Abstract

Aim: The aim of the present study was to analyze the patterns of pelvic and para-aortic lymph node involvement among our patients with early endometrial cancers.

Methods: All patients with stage I endometrial cancer (clinical and radiological) who had undergone surgical staging at Bihar cancer surgical Hospital, Malahi pakri chowk, Patna, Bihar, India were included in the study. A total of 100 patients were included in the study. Surgical and pathological data of these patients were collected and analysed retrospectively

Results: Mean age of the patients was 55 years (25–75 years). Endometrioid carcinoma was the commonest histological type (82 patients, 82%). Majority of patients (55 pts, 55%) had low-grade disease (endometrioid carcinoma grades 1 and 2) and 45 (45%) had high-grade disease (included endometrioid carcinoma grade 3, clear cell carcinoma, uterine papillary serous carcinoma and adenosquamous carcinoma). Among the patients with > 50% myometrial invasion, lymph node involvement was noted in 10 (20%) and in patient with < 50% myometrial infiltration, lymph node involvement was 7.5% (3/40) (P value 0.001). Among 90 patients without peritoneal disease, 16.66% (15 patients) had lymph node metastasis, whereas among 10 patients with peritoneal disease, 50% (5/10) had lymph node metastasis (P value 0.05). Isolated para-aortic lymph nodal metastases were noted in 4.

Conclusion: The result of STATEC (Selective Targeting of Adjuvant Therapy for Endometrial Cancer) may give a final answer regarding therapeutic benefit of lymphadenectomy in early endometrial cancer.

Keywords: Cancer endometrium, Lymphadenectomy, Sentinel lymph node mapping, Isolated para-aortic node metastasis, Complications

Introduction

Endometrial cancer (EC) is known as a common female genital malignancy with rapidly increasing incidence these years. In 2021, there will be an estimated 66,570 new cases and 12,940 deaths, making uterine cancer the second most prevalent cancer in women in U.S. after breast cancer. [1] Surgery is the mainstay for treatment include total hysterectomy + bilateral salpingooophorectomy + pelvic lymphadenectomy +/− para-aortic lymphadenectomy (TH+BSO+ PLAD+/− PALAD). LAD represents a significant component of comprehensive staging for

patients with EC. However, studies have revealed that LAD may not be conducive to the prognosis of EC patients. [2,3]

Most endometrioid endometrial cancers are confined to the uterus at diagnosis, but˜15% of apparent early stage cases have occult metastases and are destined to develop recurrence. Surgical staging, including selective lymphadenectomy, facilitates identification of patients who have metastatic disease. The decision to perform selective lymphadenectomy generally is made intraoperatively based on known risk factors such as histologic grade and depth of myometrial invasion. The risk of pelvic lymph node metastases is >10% in patients with cancers that are poorly differentiated or that invade the outer half of the myometrium. [4] Surgical staging facilitates individualization of adjuvant therapy by identifying those at highest risk of recurrence. In addition, there is some evidence that surgical resection of nodal metastases may have a therapeutic benefit. [5]

Although several risk factors for nodal metastasis have been identified, they have a low positive predictive value in clinical practice. In addition, preoperative radiologic testing using ultrasound, [6] computed tomography, [7] or magnetic resonance imaging [8] is suboptimal in identifying patients with pelvic or paraaortic nodal metastases. These radiologic studies are much more accurate in the identification of patients with a low rather than high likelihood of nodal metastasis. Elevated CA 125 levels are associated with lymph node metastasis, [9] but abnormal values occur most often in those with nonendometrioid cancers in which surgical staging is standard practice irrespective of other features. [10,11] Identification of an accurate test predictive of node metastasis in endometrial cancer would have potential clinical applications. Endometrial cancer patients with a preoperative test predictive of node metastasis could be referred to a subspecialty gynecologic oncologist, whereas patients with a low likelihood of node metastasis could be managed by the general obstetrician/ gynecologist. Improvements in referral patterns would be a more effective use of health care resources.

Incidence of lymph node metastasis is related to grade of the tumour, depth of myometrial infiltration and peritoneal disease. [12] Various scoring systems have been developed using these factors for deciding on lymph node dissection and adjuvant treatment. [13]

The aim of the present study was to analyze the patterns of pelvic and para-aortic lymph node involvement among our patients with early endometrial cancers.

Materials and Methods

All patients with stage I endometrial cancer (clinical and radiological) who had undergone surgical staging at Bihar cancer surgical Hospital, Malahi Pakri Chowk, Patna, Bihar, India were included in the study. A total of 100 patients were included in the study for one year

Methodology

Surgical and pathological data of these patients were collected and analysed retrospectively. Preoperatively, all patients had clinical evaluation to rule out intra-abdominal, cervical, vaginal and parametrial extension of the tumour. Magnetic resonance image (MRI) of abdomen and pelvis was done as an institutional protocol for all patients preoperatively to assess extent of disease in the pelvis and abdomen including retroperitoneal lymph nodes. Surgical staging included total abdominal hysterectomy, bilateral salpingooo phorectomy and bilateral pelvic lymphadenectomy with or without para-aortic lymphadenectomy. Prophylactic antibiotics was given with first generation cephalosporin (cefazolin) and metronidazole one dose 30 min before

incision (just before induction of anaesthesia) and one dose 6 h later. Pelvic lymphadenectomy included removal of bilateral iliac and obturator group of lymph nodes.

Para-aortic node dissection included removal of nodal tissue anterior to aorta and inferior vena cava up to inferior mesenteric artery. If during surgery, enlarged nodes were detected, para-aortic area node dissection was extended up to the level of left renal vein. Postoperatively, pelvic drain was removed on second postoperative day irrespective of the quantity of drain if it is not chylous. Thromboembolic prophylaxis was given with thromboembolic device (TED) stockings from 1 day prior to surgery and was continued till date of discharge. In addition, low molecular weight heparin (LMWH) injection was started 12 h after surgery, followed by daily once injection till discharge and early ambulation. Incidence of lymph node metastasis and its relation to grade of the tumour, extent of myometrial infiltration and presence of peritoneal disease were calculated.

Statistical Analysis

Continuous variables were expressed as mean and standard deviation and categorical variables as counts and percentage. Chi-square test was used to find out the significance of the factors related to frequency of positive lymph nodes. A p value < 0.05 was set for statistical significance. Statistical analysis was performed using SPSS ver. 11.0 (SPSS Inc., Chicago, IL, USA).

Results

Table 1: Clinico-pathological characteristics

Total number of patients	100
Mean age (years)	55 (25–75 years)
Menopausal status	
Pre-menopausal	15 (15%)
Post-menopausal	85 (85%)
Histology Endometrioid carcinoma	82 (82%)
Low-grade disease	
Endometrioid grade	5 (5%)
Endometrioid grade 2	50 (50%)
High-grade disease	
Endometrioid grade 3	25 (25%)
Clear cell carcinoma	15 (10%)
Papillary serous carcinoma	2 (2%)
Adenosquamous carcinoma	2 (3%)
Myometrial infiltration	
Nil	10 (10%)
< 50%	40 (40%)
> 50%	50 (50%)
Peritoneal disease	
Nil	90 (90%)
Yes	10 (10%)

Mean age of the patients was 55 years (25–75 years). Endometrioid carcinoma was the commonest histological type (82 patients, 82%). Majority of patients (55 pts, 55%) had low-grade disease (endometrioid carcinoma grades 1 and 2) and 45 (45%) had high-grade disease (included endometrioid carcinoma grade 3,

clear cell carcinoma, uterine papillary serous carcinoma and adenosquamous carcinoma).

Table 2: Frequency of lymph node metastasis and histological grade

Histology	N	No metastasis	Pelvic node metastasis	Pelvic + paraaortic node metastasis	Isolated para-aortic metastasis
Endometrioid					
Grade 1	5	4	0	0	1
Grade 2	50	40	7	1	2
Grade 3	30	20	7	2	1
Papillary serous carcinoma	3	2	1	0	0
Clear cell carcinoma	10	12	1	1	0
Adenosquamous carcinoma	2	1	1	0	

Pattern of lymph node metastasis was correlated with grade of the tumour.

Table 3: Frequency of lymph node metastasis with respect to myometrial infiltration

Myometrial infiltration (MI)	No metastasis	Pelvic node metastasis	Pelvic + para-aortic node metastasis	Isolated para-aortic node metastasis	Total
Nil	7	1	0	2 (20%)	10
< 50%	37	2 (5%)	1 (2.5%)	0	40
> 50%	35	10 (20%)	3 (6%)	2 (4%)	50

Among the patients with > 50% myometrial invasion, lymph node involvement was noted in 10 (20%) and in patient with < 50% myometrial infiltration, lymph node involvement was 7.5% (3/40) (P value 0.001).

Table 4: Lymph node metastasis with respect to peritoneal disease

Peritoneal disease	N	No metastasis	Pelvic metastasis	Pelvic + para-aortic	Paraaortic
Absent	90	80	15	2	3
Present	10	5	3	1	1

Among 90 patients without peritoneal disease, 16.66% (15 patients) had lymph node metastasis, whereas among 10 patients with peritoneal disease, 50% (5/10) had lymph node metastasis (P value 0.05). Isolated para-aortic lymph nodal metastases were noted in 4.

Table 5 Perioperative complications

Complications	20 (20%)
Mortality	1 (1%)
Intraoperative complications	8 (8%)
Major vessel injury	
Inferior vena cava	2 (2%)
External iliac vein	1 (1%)
Nerve injury	
Obturator nerve	1 (1%)
Chyle leak	3 (3%)

Postoperative complications	12 (12%)
Pelvic abscess	1 (1%)
Vault cellulitis	1 (1%)
Hematoma evacuation (pelvic)	2 (2%)
Pneumonitis	3 (3%)
Febrile morbidity	1 (1%)
Pulmonary embolism	1 (1%)
Paralytic ileus	4 (4%)
Myocardial infarction	1 (1%)

Major intraoperative vascular injury was noted in 3 (3%) patients and obturator nerve injury in 1 (1%). Other main peri-operative complications included pneumonitis in three patients, paralytic ileus in four patients. The median hospital stay was 7 days.

Discussion

Endometrial cancer (EC) is the most common malignancy of the female reproductive tract and the fourth most common cancer overall, with approximately 300,000 new cases worldwide. [14] The standard surgical approach for stage I EC consists of total hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy, which continues to be a topic of controversy in early-stage EC.

The therapeutic benefit of lymph node dissection in early endometrial cancer still remains controversial. Assessment of nodal involvement will help in accurate staging and to decide on adjuvant treatment. Preoperative MRI will help to assess degree of myometrial invasion and select out patients at low risk for nodal disease along with the grade of the tumour assessed on the biopsy.

The overall incidence of lymph node metastasis was 15% (15/100) in our study in par with the reported incidence ranging from 3 to 5% for well-differentiated tumour with superficial myometrial infiltration to 20% in poorly differentiated deep myometrial invasion. [15-17] Our data also shows a higher incidence lymph node metastasis of 22.22% (10/45) in high-grade tumours. The incidence of isolated para-aortic metastasis was 3.2% as in other studies 2–6%. [18]

Significant correlation of lymph node metastasis was found with depth of myometrial infiltration (p value 0.001) and presence of peritoneal disease (p value 0.05). Grade of the tumour alone was not significantly associated with lymph node metastasis (P value 0.455). Many of the centres practice selective lymph node dissection in endometrial cancer by risk stratification. Preoperative tumour grade in endometrial biopsy and myometrial infiltration by imaging are being used for risk stratification, and lymphadenectomy is done only in high-risk groups (patients with > 50% myometrial infiltration and high-grade disease). This practice can cause missing of lymph node metastasis in some patients with low-risk disease though it is rare.

In our study group, complications were observed in 20% (20/100) of patients. Major intra-operative and post-operative complications were noted in 8% (8/100) and 12% (12/100) of patients, respectively. Complication rates are similar to the other reports in the published literature. [19] Median hospital stay of patients was 7 days. The major postoperative complication needed increased hospital stay to 10–14 days. Now, the practice changed to start thromboprophylaxis with LMWH also on preoperative day itself as a part of ERAS (enhanced recovery after surgery) protocol.

The concept of sentinel lymph node mapping (SLNM) is the upcoming approach for lymph node evaluation to decrease the morbidities associated with lymphadenectomy. In SLNM, cervical injection alone may be associated with chance of missing the para-aortic node metastasis. Studies have shown that injecting dye into cervix and fundus improves detection rate of sentinel para-aortic nodes. [20] But at centres where sentinel lymph node mapping is not available, omitting lymphadenectomy by risk stratification should be done carefully. Even in low-risk patients, nodal basins should be evaluated intraoperative and any suspicious nodes should be biopsied. [21]

Conclusion

The result of STATEC (Selective Targeting of Adjuvant Therapy for Endometrial Cancer) may give a final answer regarding therapeutic benefit of lymphadenectomy in early endometrial cancer. Till further developments in preoperative assessment of the lymph node status based on biological factors, it is better to have an assessment of the lymph nodes for all patients with endometrial cancer depending on the available resources to prevent understaging and under treatment.

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