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ORIGINAL ARTICLE

Practical Aspects of Lymph Node Dissection in Gynecological Malignancy

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ABSTRACT

Background: In the latest years, we observe a redefinition of the role carried out by the surgery in the oncological gynecology. The astonishing technical progresses both in surgery and in intensive anesthetic therapy have made possible the development of specific surgical techniques more and more radical. Among the latest surgical techniques developed, the lymph node dissection is involved. The profits of LND in gynecological cancers have either not been studied systematically or are not as remarkable as the rate of its use would suggest. The current work aim to evaluate the role of lymph node dissection in case of gynecological malignancies **Methods:** 48 patients with different gynecological cancers were included in the study. Lymph node dissection was done for all cases Data were recorded regarding therapeutic, diagnostic benefits of LND and any morbidity or mortality related to procedure. **Results** In this study, an overall positivity rate of 45.8% was found. That a median of 26 nodes can be collected from the pelvic area and 9 nodes from the para-aortic region. This study showed that 72.7 % of patients had 3-10 positive nodes, and that the obturator group is a major route for lymphatic spread in cervical and the external iliac group is a major route for lymphatic spread in endometrial carcinoma aortic nodes were most commonly involved with ovarian carcinoma 42.7% of patients with para-aortic node metastases had positive-pelvic The incidence rate of major vascular complications reported in this study which show no mortality and 28 cases have no complications but there is 6 patients complicated by lymphoma 6 patients with wound infection 4 patient with D.V.T and 2 patient complicated with intestinal obstruction. (4/50, 8 %). **Conclusion:** Lymph node dissection is a feasible procedure that can be conducted by different techniques and it has therapeutic and prognostic role in gynecological operations.

Keywords: lymph node dissection; gynecological malignancy; pelvic and para-aortic lymph nodes.

INTRODUCTION

Evaluation of lymph nodes state is a main component of the surgical staging procedure in several gynecological malignancies

Rational for lymph node dissection changes among different gynecological cancers [1].

(1) Cervical cancer: Treatment failures which occur among patients with locally advanced disease are due to, the fact that clinical staging of cervical cancer is accurate in only 60% of cases. Undiagnosed para-aortic lymph node metastases negatively affect prognosis with 3- and 4- year overall survival rates of 39 and 29% respectively [2].

Imaging modalities determine the extent of the disease before therapy Nevertheless, the sensitivity and specificity of computed tomography (CT) was only 34 and 96% respectively.

Given the importance of lymph node metastasis to overall survival, some clinician perform a staging lymphadenectomy before anticipated combination chemotherapy and radiation, although this practice stays controversial **[1].**

(2)Endometrial cancer: After 1998 FIGO change from clinical to surgical staging including pelvic & para aortic lymphadenectomy **[2].**

Involvement of lymph nodes, significantly worse disease . While knowledge of their presence may alter treatment approaches [3].

(3)Ovarian cancer: Primary cytoreductive surgery has been an essential part of the treatment of advanced ovarian cancer, maximal surgical cytoreduction is one of the most powerful determinants of cohort survival in (FIGO) stage III IV ovarian cancer [4].

Retroperitoneal lymph node involvement takes place in approximately 50% to 80% of women with advanced ovarian cancer. In 2004, the FIGO staging included a substage for node involvement due to its prognostic significance [5].

Retrospective studies have suggested a clinically significant survival advantage following systematic lymphadenectomy in patients submitted to cytoreductive surgery for advanced disease [6].

(4) vulval cancer: lymph node metastasis was the most important prognostic factor . In 2009, FIGO modified the staging of vulval carcinoma from a clinical to a clinico-pathological staging [7].

The current work aim to evaluate the role of lymph node dissection in case of gynecological malignancies

METHODS

After IRB approval, Sample size was calculated by open EPI to be 48 cases with confidence level 95% and power of test 80%.This cross sectional study was conducted between July, 2016 till July, 2018 in obstetric and gynecology surgery departments in Zagazig university and national cancer institute Cairo University. All Patients candidate for lymphadenectomy with different gynecological malignancies were included in the study. Patients with BMI>40 and inoperable cases were excluded from the study. All patients were subjected to a detailed history, examination (general, abdominal and local) and investigation (laboratory, imaging, biobsy etc). Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work is carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Operative Technique: - General anesthesia
- Supine position - Vertical midline incision.

Surgical technique:

Pelvic lymphadenectomy Incising the peritoneum after ligation of round ligament . The para rectal and para vesical spaces were developed . The dissection continued until the circumflex iliac vein is clearly visualized.

The surgeon then dissected within the obturator fossa. until the obturator nerve was visualized.

Systematic para-aortic lymphadenectomy: The peritoneum was incised in front of the aorta down to the common iliac arteries. A plane developed between peritoneum and great vessels (Aorta & IVC) and was extended laterally to ureters on each side. The node-beating areolar tissue in front of the aorta was incised .The limits of the dissection were the bifurcation of the aorta inferiorly, the proximal part of the common iliac artery infero-laterally and the ureters laterally. The superior extent of the dissection was renal vein.

The resected lymphatic tissue was grouped and labeled

These data were calculated and analyzed (operating time, blood loss and procedure related complications).

RESULTS

Table(1) shows that age of the study group was (52.9±10.3) ranged from (31to 70) years, twenty five (52.1%) of them had ovarian tumor,

(47.9%) had stage II, (45.8%) had positive LN involvement, (39.6%) had figo stage I, (43.8%) had figo grade well and (29.2%) were pelvic in site.Table(2) show that the operation time in the study group was (206.7±25.7) ranged from (180 to 260) hours, blood loss was (328.1±94.4) ranged from (200-550) (*ml)*, drain duration was (7.5±1.4) ranged from (5-10) days and hospital stay was (4.1±0.8) ranged from (3-5) days.
Table(3) show that there was statistically significant difference between patients with ovarian, cervical and endometrial tumors in pelvic, external, common, internal iliac, obturator LNs which were more common in cervical tumors and aortic LNs were more common in ovarian tumors.Table(4) show that (58.3%) of the study group had no postoperative complications, infections and lymphocyte were the same (12.5%) while DVT and obstruction were (8.3%). Regarding intraoperative complications, only (4.1%) had intestinal obstruction

Table (1): Age and tumor characteristics of the study group:

Variable	The case group(48) mean ± SD (Range) median	
Age (years):	52.9±10.3 (31-70) 53	
Variable	**NO(48)**	**%**
Tumor		
Cervix	12	25.0%
Ovary	25	52.1%
Endometrium	11	22.9%
Stage		
I	12	25.0%
II	25	52.1%
III	11	22.9%
LN		
Positive	22	45.8%
Negative	26	54.2%
Figo stage		
I	19	39.6%
II	17	35.4%
III	12	25.0%
Figo grade		
Poor	14	
Moderate	13	29.1%
Well	21	27.1%
		43.8%
Site		
Negative	26	54.2%
Aortic	4	8.3%
Pelvic	14	29.2%

Both	4	8.3%

Table (2): Operative data of the study group:

Variable	The case group(48) mean ± SD (Range) median
Operation time ***(Hours):***	206.7±25.7 (180-260) 200
Blood loss **(*ml*)**	328.1±94.4 (200-550) 350
Drain duration **(*day*)**	7.5±1.4 (5-10) 8
Hospital stay **(*days*)**	4.1±0.8 (3-5) 4

Table (3): Median number and site of lymph nodes removed according to type of tumor in the study group:

Variable	*Cervix* No.(12) *Median* *(range)*	*Ovary* No.(25) *Median* *(range)*	*Endometrium* No.(11) *Median* *(range)*	Kruskal Walis test	p-value
Pelvic **No.**(61)	29 (15-31)	16 (10-21)	16 (7-17)	37.8	**0.001****
Common iliac **No.**(20)	9 (8-14)	6 (4-12)	5 (4-11)	10.1	**0.001****
External iliac **No.**(11)	5 (4-9)	3 (2-8)	3 (2-7)	4.9	**0.01***
Internal iliac **No.**(9)	4 (2-7)	3 (2-6)	2 (2-4)	4.8	**0.01***
Obturator **No.**(21)	11 (4-16)	4 (5-9)	6 (5-10)	3.1	**0.03***
Aortic **No.**(13)	2 (5-14)	7 (4-12)	4 (4-11)	5.4	**0.008***

* Statistically significant difference ($P \leq 0.05$)

* *Statistically highly significant difference (P ≤ 0.001)

Table (4): Intra-operative and post-operative complications in the study group:

Variable	No.(48)	%
Intra-operative complications		
No	46	95.9%
Intestinal injury	2	4.1%
post-operative complications		
NO	28	58.3%
DVT	4	8.3%

DISCUSSION

For appropriate staging of gynecological malignancies, thorough exploration of the retroperitoneal space is mandatory to detect metastasis of pelvic and para-aortic lymph nodes. It would be important in planning surgery to help expect the possibility of retroperitoneal lymph node positivity preoperatively. Nowadays, methods utilized for the assessment of lymph nodes are different and ineffective. However, data on how thoroughly these methods predict lymph node positivity are rare. We found that CT, extensively employed for the assessment of para-aortic lymph nodes, failed to detect most metastatic nodes, with a sensitivity of 16.7%.

Blythe et al.**[8]** stated that para-aortic lymph node biopsies should be included in the routine evaluation of patients with gynecological malignancies.

Onda et al. **[9]** stated that aortic lymph nodes above the inferior mesenteric artery and the internal and external iliac and obturator lymph nodes are essential sites for lymph node biopsy in ovarian carcinoma. However, the appropriate method of biopsy for assessing lymph node involvement in gynecological malignancies has yet to be identified.

In this study, an overall positivity rate of 45.8% was found. According to the results of several studies, pelvic nodes were involved in 18% to 55% and para-aortic nodes in 10% to 40% of all patients when complete nodal dissections were performed. It is claimed that a radical pelvic lymphadenectomy should yield at least between 9 to 37 nodes and para-aortic lymphadenectomy between 5 to 12 nodes, respectively **[9]**.

Our investigation pointed out that a median of 26 nodes can be collected from the pelvic area and 9 nodes from the para-aortic region. Most published studies have reported a smaller number of nodes because only suspicious nodes were removed. Despite individual differences, surgical oncologist should be aware that, as in axillary lymph node dissection for breast cancer, systematic pelvic and aortic lymphadenectomy requires a minimum number of collected nodes and parameters to standardize lymphadenectomy must be set **[11].** The number of node groups and nodes removed indicates the accuracy of the procedure **[12]**.

Therefore, the data collected should indicate the number and pattern of lymphatic spread for gynecologic malignancies with a higher precision **[13]**.

This study showed that 72.7 % of patients had 3-10 positive nodes, and that the obturator group is a major route for lymphatic spread in cervical which comes in agreement with Panici et al.**[14]** and ovarian which agree with Onda et al .**[9]** carcinomas and the external iliac group is a principal route for lymphatic spread in endometrial carcinoma which agree with Mariani et al **[15].**

Moreover, aortic nodes were most commonly involved with ovarian carcinoma in accordance with most published series **[16,17].**

Para-aortic node metastasis was found in 70% of the patients with pelvic node involvement **[18]**. In the current study, 42.7% of patients with para-aortic node metastases had positive-pelvic nodes, in accordance with other reports **[13]**.

However, para-aortic spreads have skipped the pelvic region in 4.3%. Thus, lymph node assessment should include both the aortic and pelvic lymph nodes in agreement with recently published series **[19].**

Concerning radiological detection of nodal metastasis, although imaging modalities are improving accuracy, there has been no large prospective trial demonstrating the comparability of any imaging modality compared to surgical evaluation of lymph nodes **[20].**

In a meta-analysis of studies evaluating computed tomography (CT) scan and magnetic resonance imaging (MRI) efficacy for assessing nodal status in cervical cancer patients, the authors concluded that these methods have only moderate sensitivity and specificity in detecting nodal metastases **[21].**

Particularly, CT scan and MRI are relatively inaccurate in detecting small volume of disease in lymph nodes: suspicion is mainly raised when lymph node diameter is greater than 1 cm. Most metastatic lymph nodes, however, will not meet this size criterion and therefore will go undiagnosed **[22].**

Currently, even if (18) F-fluorodeoxyglucose positron emission tomography (PET) scanning is recognized better at detecting microscopic node spread than other modalities, in a recent series it has demonstrated to be a feeble predictor of nodal involvement with an overall sensitivity of 38% and a positive predictive value of 56%**(13)**. The results were clearly related to the size of involved nodes with detection slightly increasing when metastases were N 10 mm, making questionable the routine use of PET scan as the only decision-making tool in this setting of patients **[21].**

In addition, the Gynecologic Oncology Group (GOG)-0233/American College of Radiology Imaging Network (ACRIN)-6671 ongoing trial is going to assess the efficacy of preoperative FDG-PET/CT and Ferumoxtran-10 (an ultra-small particle iron oxide — "USPIO" agent) MRI scanning to primary chemo radiation therapy to detect nodal metastasis in patients affected by locally advanced (IB2–IVA) carcinoma of the cervix**[21].**

The benefit of lymphadenectomy has been extensively demonstrated in several retrospective series reporting improved survival mostly for patients after debulking of grossly involved nodes, and similar survival for patients with completely resected lymph nodes has been reported whether microscopically or macroscopically involved **[20].**

There is now an outstanding evidence of the undoubtful need to proceed resecting pelvic nodes up to the level of common iliac sites, and also aortic nodes in case of pelvic node disease detected intraoperatively, due to the high incidence of lymphatic upper spread in such patients.

When a systematic pelvic lymphadenectomy is rationally indicated, evidence suggests that it should be performed safely and in a standardized way by a gynecologic oncologist, with 25–35 nodes recovered in order to consider adequate the procedure, while 12–25 aortic nodes in case of para-aortic lymph nodes dissection**[22].**

The pattern of lymphatic spread should form the basis for establishing the criteria for a

systematic lymphadenectomy with curative possibility. When a therapeutic intent is pursued, the pattern of lymphatic metastasis suggests that a systematic dissection of all the lymphatic tissue located around the cervix and the pelvic vessels should be performed in patients with both early stage and locally advanced disease in order to remove the potential sites of metastasis entirely, while systematic aortic lymphadenectomy should be performed in cases of pelvic nodes involvement. In case of no diseased upper pelvic (common iliac) and aortic nodes, patients may be spared of the costs, side effects and complications of an unnecessary extension of external radiation field. Conversely, patients with microscopically positive lymph nodes may benefit from adjuvant chemotherapy or extended field radiation **[20].**

Finally, patients with macroscopically diseased lymph nodes mostly benefit from surgical complete debulking, also considering the reported limited effect of radiation in these cases**[23].**

The present report shows that systematic pelvic and para-aortic lymphadenectomy could be carried out with an acceptable morbidity and no mortality**[21].** Among the postoperative complications, the development of lymphocyte was the most frequent and troublesome **[23].**

The incidence rate of major vascular complications reported in this study (4/50, 8%) is comparable to that which occurred in other series[(20)], although vascular injuries did occur, there were no permanent sequelae. Moreover, as the surgical team acquired experience, the operating time and the blood loss gradually diminished in accordance with other reports **[23].**

In which this results agree with this study which show no mortality and 28 cases have no complications but there is 6 patients complicated by lymphoma 6 patients with wound infection 4 patient with D.V.T and 2 patient complicated with intestinal obstruction.

This series demonstrated, as do those of other authors, that metastatic pelvic and para-aortic nodes are important prognostic factors. Recently, large studies reported that patients who underwent lymphadenectomy had a better survival than patient in which node dissection was not performed **[21].**In this study there is no detection of survival as the present study only for 2 years and for detection of optimum survival the study should be contained to 5 years at least but in this study 11 patients was positive inspite of there was negative by our conventional methods C.T and M.R.I which upgrade staging and affect the treatment plane.

CONCLUSION

Systematic pelvic and para-aortic lymphadenectomy represents the only reliable method for the assessment of lymphatic spread in gynecologic oncology, given the low accuracy of the imaging techniques. Systematic pelvic and aortic lymphadenectomy is an effective procedure and can be carried out with acceptable morbidity and no mortality. However, to provide strong evidence that this procedure has a therapeutic benefit, randomized controlled studies are needed.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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