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RESEARCH ARTICLE

Evaluation of pelvic lymph node dissection in endometrial carcinoma

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ABSTRACT

Background: Pelvic and para-aortic lymphadenectomy is suggested to provide prognostic and therapeutic benefits in endometrial carcinoma, particularly in high-risk and advanced tumors. **Aim**: Herein we compare the oncological and surgical outcomes in patients with and without pelvic lymphadenectomy performed. **Patients and Methods:** A retrospective study, included endometrial carcinoma patients who underwent hysterectomy at National Cancer Institute, Egypt from January 2013 to December 2017. We divided the patients into two groups according to the documented operative details, one group was subjected to pelvic lymphadenectomy (PLN), and one group had no lymphadenectomy done (No PLN). **Results**: 90 patients (60 patients had PLN, 30 patients had no PLN). The death rate was higher in the No PLN group compared to the PLN (36.7% vs 20%). The mean overall survival (OS), and disease-free survival (DFS) were nearly equal in both groups. Retroperitoneal nodal recurrence occurred in 6 patients in the PLN group out of 18 recurrences (33.3%) and in 5 patients in the no PLN group out of 11 recurrences (45.5%) with a p-value=0.869. The 5-year DFS in PLN and No PLN groups was 50% and 26.7% respectively, and the 5-year OS in PLN and No PLN groups was 70%, and 60**%,** respectively but statistically not significant. Early postoperative complications occurred in 24 patients (40%) in the PLN group and 12 patients (40%) in the No PLN group. **Conclusion:** Excluding patients with low risk for nodal disease in endometrial carcinoma, pelvic lymphadenectomy may have a positive impact on survival or recurrence patterns.

Keywords: Endometrial carcinoma; Pelvic lymphadenectomy; Para-aortic Lymphadenectomy; Extended lymphadenectomy

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INTRODUCTION

In developed nations, endometrial carcinoma (EC) is the most prevalent in female genital tract malignant tumors (Koskas et al., 2021). Because surgical staging has numerous positive diagnostic, prognostic, and therapeutic effects for these patients, current worldwide recommendations recommend it as a primary treatment policy for all forms of EC (Bohîlțea et al. 2015).

Pelvic lymphadenectomy is an essential part of surgical staging. The caudal part of the common iliac artery, the external iliac artery, the deep circumflex iliac vein, and the obturator pad of fat are all included in the pelvic lymphadenectomy. The inferior vena cava and aortic nodal tissue is removed during a para-aortic lymphadenectomy (up to the renal vessels or the inferior mesenteric artery) (Mahdy et al., 2022). Giving to the updated FIGO staging system for EC, the lone approach to identify patients with FIGO stage IIIc disease is through lymphadenectomy. As a result, lymphadenectomy delivers critical information about the necessity for adjuvant treatment, allowing for improved survival and a reduction in the morbidity of over-treatment (radiation or chemotherapy effects) as well as the risks of under-treatment (recurrence) (Robboy et al. 2017). Apart from clinical trials, lymphadenectomy is not advised for individuals with early-stage type (I) EC since it has little if any impact on overall and disease-free survival.

Contrarily, in patients with type (I) EC at advanced stages and in type (II) EC patients, lymphadenectomy has been shown to improve overall survival (Robboy et al. 2017). Although there is no agreement on the number of dissected lymph nodes, the harvesting of at least 10 nodes is associated with a better prognosis. Therefore, the entire number of removed lymph nodes reveals how adequate was lymphadenectomy. However, extended lymphadenectomy (more than 14 lymph nodes) rises considerably the morbidity rates (such as vascular or nerve injury, and lymphedema). Surgeons should then balance the morbidity risk versus the survival benefit regarding the extent of lymphadenectomy (Mahdy et al., 2022).

We aimed at studying the surgical (postoperative complications) and oncological (recurrence and survival) outcomes in endometrial carcinoma patients who underwent pelvic lymphadenectomy and compare them to those who had no lymphadenectomy done.

PATIENTS AND METHODS

Ethical Approval, patients' risks, confidentiality, and consent to Participate

The study is retrospective and poses no harm to patients; all data have been made anonymous to protect the privacy and confidentiality of patient information. The study was approved by the Institutional Review Board (IRB) of the National Cancer Institute, Cairo University-Egypt in session 133, dated 11.03.2019, IRB number # 201819013.

This study included all patients with primary endometrial carcinoma who underwent total abdominal hysterectomy at the National Cancer Institute, Cairo University, Egypt from January 2013 to December 2017. We had a total of 122 patients. Only 90 patients were included in our study, and we excluded 32 patients whose files were missed, or whose essential data were not documented including operative details. Based on the operative details, we found a part of the patients had undergone pelvic lymph node dissection, the other part had no pelvic lymph node dissection. Those who had no pelvic lymph node dissection were found to be high-risk patients (Type 2, Invasion of more than half of myometrium, and reaching to endocervix). So, we had two groups allocated; the group of pelvic lymph node dissection (PLN), and the group of No pelvic lymph node dissection (No PLN).

All patients` files were reviewed, and the following data were obtained: date, of diagnosis, age, gender, main complaint, tumor grade, stage, laboratory results, radiological data, biopsy results, date of surgery, operative details, postoperative complications, and final pathology, follow-up data (recurrence, and survival). Overall survival (OS) was calculated as the interval from diagnosis to death or last follow-up. Disease-free survival (DFS) was the interval from surgery to recurrence, death, or last follow-up**.**

Statistical analysis

Data were analyzed using SPSS 21(Statistical Package of Social Sciences). Numerical data were defined as mean and standard deviationor median and range, as proper. Categorical data were labeled as numbers and percentages. Numerical variables were tested using t-test or Mann Whitney as proper and categorical variables were tested using chi-square or Fisher exact test as proper. Survival analysis was done using the Kaplan-Meier method. Predictor and prognostic variables were related to survival using the log-rank test. Cox regression analysis was done to assess independent prognostic variables affecting OS and DFS time. P value set significant at 0.05 levels. All tests weretwo-tailed.

RESULTS

This study was conducted on 90 patients [60 patients underwent pelvic lymphadenectomy (PLN), and 30 patients had no PLN]. In the PLN group, the mean age was 55.55 ± 8.48 years (range: 35-67), and the mean body mass index (BMI) was 26.9 ± 1.05 kg/m^2 (range: 25-29). In the No PLN group, the mean age was 54.97 ± 8.92 years (range: 35-67), and the mean body mass index (BMI) was 26.9 ± 0.94 kg/m^2 (range: 25-29). We had no significant differences between both groups regarding these two items (p-value= 0.763 and 0.884). Also, there was no significant difference between both groups regarding tumor size. In the PLN group, the

mean tumor size was 3.89± 0.85 cm (range: 2.4-5.5), and in the No PLN group, the mean size was 3.91±0.93 cms (range: 2.4-5.5) with a p-value of 0.912.

The most common histologic type in both groups was theendometrioid type, however, no significant differences were present between both groups regarding histological types. The most common tumor grade in the PLN group was grade I (45%), while in the No PLN group was grade II (50%); yet with no statistically significant differences. The least common was grade III in both groups as shown in table 1. Both groups were comparable regarding the tumor stage, where the commonest stage was stage I, and the least common was stage III in the two groups with an insignificant p-value. The recurrence rates were comparable in both groups. The death rate was higher in the No PLN group than in the PLN (36.7% vs 20%), yet statistically not significant, as illustrated in Table 1. The mean overall survival (OS), and disease-free survival (DFS) were nearly equal in both groups as shown in Table 2.

Retroperitoneal nodal recurrence occurred in 6 patients in the PLN group, out of 18 recurrences representing 33.3%, while it occurred in 5 patients in the no PLN group out of 11 recurrences and thus represents 45.4%. However, this was not statistically significant (p-value=0.87). Other recurrent sites are shown in Figure 1. The 5-year DFS and OS were much higher in the PLN group. The 5-year DFS in PLN and No PLN groups was 50 % and 26.7 %, respectively. The 5-year OS in PLN and No PLN groups was 70 %, and 60 % respectively. These differences were, however, not statistically significant (Table 3, Figure 2).

Early postoperative complications (within the 1st 30 days) occurred in 24 patients (40%) in the PLN group, and 12 patients (40%) in the No PLN group with no significant differences as shown in Table 4. Urinary bladder and ureteric injury were more evident in the PLN group. Urinary bladder injury occurred in 3 patients (5%), and zero patients in the PLN, and No PLN groups, respectively. Ureteric injury ensued in 6 patients (10%), and in 2 patients (6.7%) in the PLN, and No PLN groups, respectively.

Most early complications were managed conservatively and fully recovered. Two of the ureteric injury cases were managed by double J stent insertion cystoscopically. Late complications occurred in 9 patients (15%) in the PLN group, and 8 patients (26.7%) in the No PLN group, without significant differences. Burst abdomen cases were strangely evident later than what is usually expected, and they were managed surgically as shown in Table 4. The mean number of retrieved lymph nodes in the PLN group was 25.2 ± 9.53 nodes (range: 12-50) with a median of 24.

DISCUSSION

Endometrial carcinoma treatment has significantly evolved over the last 25 years. A wide range of practices concerning lymph node assessment during staging is present, which varies from nothing to sentinel lymph node (SLN) mapping to total pelvic and paraaortic lymphadenectomy (Guo et al. 2018).

In the current study, we compared two groups retrospectively. A group underwent hysterectomy and pelvic lymphadenectomy (PLN), and a group whose tumors were high risk underwent hysterectomy without pelvic lymphadenectomy (No PLN). In the present study, the mean number of retrieved pelvic LNs in the PLN group was 25.20 ± 9.53 (range, 12-50). The number of retrieved lymph nodes in our study was higher than the number removed in different studies. Cragun et al. study stated that the median number of pelvic nodes harvested was 11 (range, 7-17) (Cragun et al. 2005). In Coronado et al study the median number was 16 nodes (range, 1–34) (Coronado et al. 2018), and Eggemann H et al. stated a median of 19 nodes was harvested (range 2–67) (Eggemann et al. 2016). In this study, the recurrence occurred mainly in no PLN in 36.7% and PLN in 30% of cases but with no significant difference. In agreement with our results, Ørtoft G et al. had no significant difference in recurrence when comparing patients with and without lymphadenectomy. This shows that pelvic lymph node recurrences can still occur even after an adequate pelvic lymphadenectomy (Ørtoft et al. 2019). The mean DFS in the PLN group was 32.6 months, and in the No, PLN was 30.37.

Table 1. Patients' and tumors' characteristics, and overall disease outcome

Patients / Tumors' Characteristic	PLN (n=60)		No PLN (n=30)		P-value
	No.	%	No.	%	
Menopause					
No	27	45	15	50	0.654
Yes	33	55	15	50	
Histologic subtype					
Mixed	3	5	1	3.3	
Clear cell	6	10	3	10	0.977
Endometroid	36	60	17	56.7	
Papillary serous	15	25	9	30	
Tumor grade					
G1	27	45	11	36.7	
G2	24	40	15	50	0.661
G3	9	15	4	13.3	
FIGO stage					
I	33	55	14	46.7	
II	21	35	13	43.3	0.728
III	6	10	3	10	
Recurrence					
Yes	18	30	11	36.7	0.523
No	42	70	19	63.3	
Death					
Yes	12	20	11	36.7	0.087
No	48	80	19	63.3	

PLN: pelvic lymphadenectomy, No PLN: no pelvic lymphadenectomy

Table 2. Overall survival (OS) and Disease-free survival (DFS) (month) of the 90 studied patients

Item	PLN (n = 60)	No PLN(n=30)	P-value
Disease Free Survival (months)			
Min. – Max.	6– 60	5– 54	
Mean ± SD.	32.6 ±14.52	30.37 ±13.92	
Median	32.5	31	0.495
Overall Survival (months)			
Min. – Max.	6 – 65	5 – 65	0.728
Mean ± SD.	47.9 ±19.75	46.2 ±20.7	
Median	60	60	

Table 3. Five-year follow-up survival data of the 90 studied patients

Follow up after 5 years	PLN (n = 60)		No PLN (n = 30)		P-value
	No.	%	No.	%	
Disease-Free Survival					
No	24	40	21	70	
Yes	30	50	8	26.7	
Lost follow up	6	10	1	3.3	0.089
Overall Survival					
No	12	20	11	36.7	
Yes	42	70	18	60	0.117
Lost follow up	6	10	1	3.3	

Table 4. Postoperative complications in the 90 studied patients

Complication type	PLN (n = 60)		No PLN (n = 30)		P- value
	No.	%	No.	%	
Early complications					1
No	36	60	18	60	
Urinary bladder tear	3	5	0	0	0.548
Ileus	18	30	8	26.7	0.742
Rectal tear	3	5	2	6.7	1
Ureteric injury	6	10	2	6.7	0.714
Wound infection	3	5	2	6.7	1
Late complications					
No	51	85	22	73.3	0.477
Lymphocele	3	5	2	6.7	
Incisional hernia	3	5	4	13.3	
Burst abdomen	3	5	2	6.7	

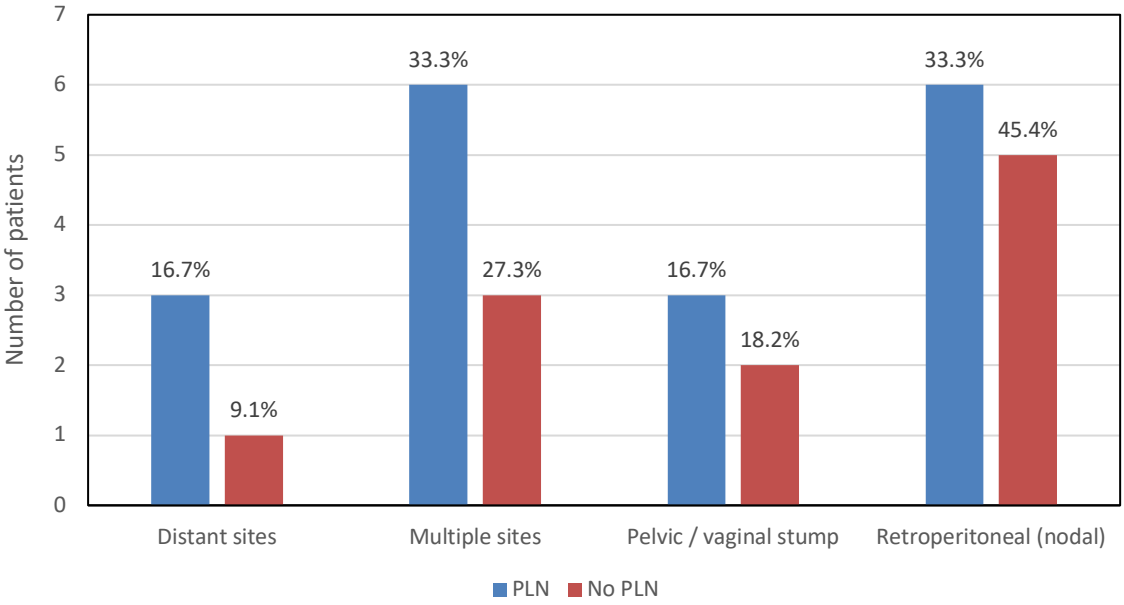

Figure 1. Comparison of the patients with and without PLN according to the site of recurrence. PLN: group of pelvic lymphadenectomy, No PLN: group with no pelvic. Lymphadenectomy. $\chi 2 = 1.4$, p-value= 0.87

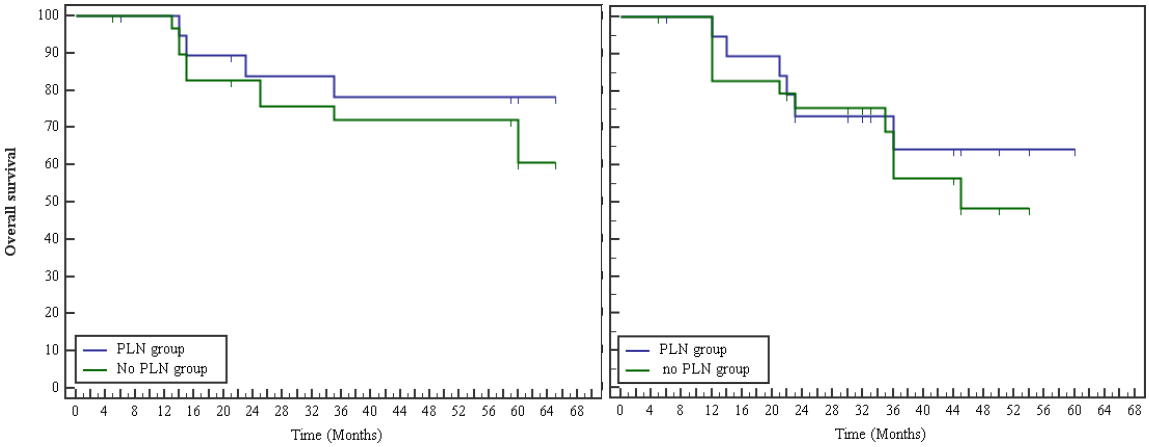

Figure 2. Overall survival (A) and disease-free survival (DFS) (B) curves of the 90 studied patients

The mean OS was 47.9, and 46.2 in PLN, and No PLN groups respectively with insignificant differences. Our study's findings concur with two randomized studies comparing patients with and without pelvic lymphadenectomy, show no differences in early-stage endometrial cancer survival or recurrence rates. However, the global better outcomes in low-risk EC patients made estimating the worth of lymphadenectomy demanding and inaccurate in these studies (Panici et al. 2008; H et al. 2009).

In contrast, advanced high-risk tumors including stage III-IV disease have shown improved outcomes, as reported in the retrospective SEPAL (Survival effect of para-aortic lymphadenectomy in endometrial cancer) study when para-aortic lymphadenectomy is added to pelvic lymphadenectomy (Panici et al. 2008; H et al. 2009; Smith et al. 2008). This was even more supported in other studies, where a national population-based study (n=42 184) confirmed an overall survival and cancer-specific survival benefit in high-stage disease if more than 11 lymph nodes were obtained (Smith et al. 2008). Another recent meta-analysis determined that when compared to pelvic lymphadenectomy, para-aortic lymphadenectomy was associated with better survival in intermediate- or high-risk cases (Guo et al. 2018). Meanwhile, in Ørtoft G et al study, para-aortic lymphadenectomy showed insignificant results. They, however, had a low number of patients (62) and a low average number (5,5) of nodes retrieved, signifying inadequate para-aortic lymphadenectomy (Ørtoft et al. 2019).

In the current study, the 5 years DFS in PLN and No PLN groups was 50%, and 26.7% respectively. Patients who lost follow-up were 10% in the PLN group, and 3.3% in the No PLN group. The 5-years Overall Survival in PLN and No PLN group was 70 %, and 60 % respectively. Data on 39 396 females with endometrioid carcinomas from the US National Cancer Institute database, compared 12 333 (31·3%) patients who underwent staging laparotomy, and lymphadenectomy, with 27, 63 patients who had no lymphadenectomy. Patients with disease stages I, II, III, and IV subjected to lymphadenectomy had 5-year disease-specific survival rates of 95.5%, 90.4%, 73.8%, and 53.3%, respectively, compared to 96.6%, 82.2%, 63.1%, and 26.9% for those not subjected to lymphadenectomy ($p>0.05$ for stage I; $p<0.001$ for stages II-IV) (Chan et al. 2007).

Another study by Coronado PJ et al showed a 5-year DFS of 79.5% in the lymphadenectomy group, and 87.4% in the no- lymphadenectomy group. DFS did not show a significant difference. Also, a similar 5-year OS in the lymphadenectomy group compared to the no-lymphadenectomy group (86.8% vs. 83.4%, respectively) (Coronado et al. 2018). In the current study, we had insignificant differences between the two groups as regard early or late complications, 20% of the PLN group died, and in No PLN 36.7% but the difference didn't reach significance. Eggemann H et al showed that death rates in those who had no lymphadenectomy done and those who underwent pelvic lymphadenectomy were 155 out of 392 (39.5 %) and 120 out of 415 (37.6 %), respectively (Eggemann et al. 2016).

Proppe and colleagues reported that patients subjected to lymphadenectomy, particularly extended form suffered complications more frequently and more severe than those who had no lymphadenectomy. In the lymphadenectomy group of the 113 patients, 97 (45.5%) had mild complications, and 16 (7.5%) had severe complications compared to 89 (41.8%), and 9 (4.2%) in the no lymphadenectomy group, respectively. Lymphatic complications were found in 14 (6.6%), 2 (0.9%) of the lymphadenectomy, and no lymphadenectomy groups with a p-value of 0.004. Drains output median discharge daily in ml was 2385±3337, and 250.3±269.2 in the lymphadenectomy and no lymphadenectomy groups respectively (Proppe et al. 2022).

CONCLUSION

Pelvic lymphadenectomy in patients with endometrial carcinoma has no great impact on survival or recurrence patterns. The benefit of lymphadenectomy is more evident in intermediate, high-risk patients, and advanced disease. Accurate establishment of the risk of nodal involvement is, therefore, essential to reduce the call for lymph node dissection in low-

risk patients to avoid its associated morbidities. Although an extended lymphadenectomy may give important prognostic data, it is only approved as an investigational element of curative intent.

AUTHOR CONTRIBUTIONS

All authors contributed nearly equally to the different steps of our study as follows: AE shared in data collection and analysis, literature research, statistical analysis, manuscript conceptualization, preparation, editing, and reviewing and shared in performing the surgeries for the patients. MT shared in data collection and analysis, literature research and statistical analysis, manuscript conceptualization, and preparation. He wrote the main draft and performed the necessary editing and reviewing, and shared in performing the surgeries for the patients. MS shared in data analysis, literature research and statistical analysis, manuscript conceptualization, editing, and reviewing and shared in performing the surgeries for the patients. NR shared in data collection and analysis, literature research, manuscript conceptualization, editing, and reviewing and shared in performing the surgeries for the patients. NEE shared in the data collection and analysis, statistical analysis, manuscript conceptualization, editing, and reviewing. IA shared in data collection and analysis, literature research, manuscript conceptualization, editing, and reviewing and shared in performing the surgeries for the patients. All authors read and approved the final manuscript.

DATA AVAILABILITY

The datasets used and/or analyzed in this study are available from the corresponding author upon request.

CONFLICTS OF INTEREST

No conflicts of interest.

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No fund was obtained

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