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ORIGINAL ARTICLE

Efficacy of laparoscopic, pelvic and para-aortic lymphadenectomy in the treatment of endometrial carcinoma

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Summary

Purpose: *To investigate the clinical efficacy and safety of laparoscopic pelvic and para-aortic lymphadenectomy in the treatment of endometrial carcinoma.*

Methods: *The clinical data of 110 patients with endometrial carcinoma were retrospectively reviewed. All patients were categorized into two groups. The pelvic lymphadenectomy (PLD) group was subjected to pelvic lymph node dissection alone, while the para-aortic lymphadenectomy (PALD)+PLD group underwent pelvic and para-aortic lymphadenectomy. The operation time, intraoperative bleeding, volume of postoperative drainage, number of resected lymph nodes, number of positive lymph nodes, and incidence of postoperative complications were compared between the two groups of patients. In addition, the tumor recurrence and survival were followed up and compared.*

Results: *The operation time was significantly longer in the PALD+PLD group than that in the PLD group (p<0.001). The average number of resected lymph nodes and the number of positive lymph nodes in the PALD+PLD group were significantly greater than those in the PLD group. The total recurrence rate was 9.1% (5/55) vs. 20.0% (11/55) between the PLD group and PALD+PLD group, indicating a statistically significant difference (p=0.045). Moreover, the recurrence rate of stage III patients was 50.0% (3/6) and 25.0% (5/55) in the PLD group and PALD+PLD group, respectively, showing a statistically significant difference (p=0.034). During the follow-up period, the 3-year overall survival (OS) was 90.9% (50/55) and 96.4% (53/55) in the PLD group and PALD+PLD group, respectively, indicating no statistically significant difference (p=0.249, log-rank test).*

Conclusion: *Laparoscopic pelvic and para-aortic lymphadenectomy for endometrial carcinoma can increase the number of resected lymph nodes and reduce the recurrence rate. Moreover, it does not increase the incidence rate of surgical complications.*

Key words: *para-aortic lymph nodes, pelvic lymph node dissection, endometrial carcinoma*

Introduction

Endometrial carcinoma is a common malignancy involving the female genital system, whose incidence rate exhibits an increasing trend annually [1]. Clinically, surgery has been accepted as a mainstay in the treatment of endometrial carcinoma, and whether to use hormone therapy, radiotherapy or other adjuvant therapy is decided based on the postoperative pathologic results [2]. At present, comprehensive staging surgery is recommended, and in addition to the whole uterus and bilateral adnexae, the surgical extent also involves bilateral pelvic lymph nodes and para-aortic lymph nodes [3,4]. Lymph node metastasis is the main risk factor for poor prognosis in patients with endometrial carcinoma, but the value and extent of lymph node resection have not yet reached a consensus [5].

In this study, the clinical data of patients with endometrial carcinoma were analyzed to explore the clinical efficacy and safety of para-aortic lymphadenectomy in the treatment of endometrial carcinoma, so as to provide scientific bases for the selection of surgical methods for these patients.

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Methods

General data

The clinical data of 110 patients with endometrial carcinoma admitted to the hospital were retrospectively reviewed. The inclusion criteria were as follows: a) newly-treated patients without combined adjuvant therapy before surgery, including chemotherapy, radiotherapy and hormone therapy; b) those who underwent surgery including extrafascial hysterectomy, extensive and sub-extensive total hysterectomy + bilateral adnexal resection; c) those diagnosed with endometrial carcinoma according to postoperative pathologic results; d) those with at least one measurable lesion; and e) those with an expected survival time of more than 3 months. The exclusion criteria involved: a) recurrent endometrial carcinoma patients without undergoing lymph node dissection; b) those with extensive pelvic and abdominal metastases or distant metastasis; c) those with pathological diagnosis of endometrial stromal sarcoma or malignant tumors in other sites; or d) those with serious underlying diseases (heart, liver, lung, kidney, *etc.*). The baseline data including age, gender, tumor stage, tumor pathologic type and Karnofsky performance (KPS) score are shown in Table 1. The study complied with the *Declaration of Helsinki*, and signed informed consent was obtained from all patients. This study was approved by the ethics committee of Jinan people's Hospital Affiliated to Shandong First Medical University (Decision no.19-CN-EA-0452JN-32).

Therapeutic methods

All patients underwent extrafascial hysterectomy, extensive or sub-extensive total hysterectomy + bilateral adnexal resection in our hospital. Pelvic lymph node dissection or pelvic and para-aortic lymphadenectomy were performed according to the patient's age, comorbidities, obesity, pathologic grade, pathologic type, imaging examination results, and sectional uterine specimens, as well as the desire of the patients and their families. The extent of pelvic lymph node dissection included internal iliac, external iliac, common iliac, obturator and deep inguinal lymph nodes, starting from 3 cm above the common iliac bifurcation, and gradually descending to the deep inguinal and obturator nerve level, inward to the internal iliac artery, and outside to the surface of the psoas muscle. It should be noted that the lymph nodes were mostly left on the side wall of the blood vessel and the space between the blood vessel walls. Para-aortic lymphadenectomy is mainly divided into dissection of low-position lymph nodes and high-position lymph nodes. The upper boundary of the high-position para-aortic lymphadenectomy area is to the level of the renal vein, and the extent of low-position lymph node dissection starts from the inferior mesenteric artery and ends at the anterior part of the sacrum. The para-aortic lymphadenectomy conducted in our hospital was low-position para-aortic lymphadenectomy. After operation, radiotherapy, chemotherapy, hormone therapy or combined adjuvant therapy were given according to the pathologic high-risk factors in the patient.

Observation indicators

The operation time, amount of intraoperative bleeding, volume of postoperative drainage and number of resected lymph nodes were recorded, and the incidence of intraoperative and postoperative complications was compared between the two groups of patients. In addition, the tumor recurrence and survival were followed up and recorded. The emergence of new lesions within

Table 1. Baseline characteristics of the studied patients

Parameters	*PLD group (n=55)* *n (%)*	*PLD+PALD group (n=55)* *n (%)*	*p value*
Age (years)	51.6±9.4	53.1±9.7	0.412
Pathological type			0.332
Endometrioid adenocarcinoma	47 (85.5)	42 (76.4)	
Others	8 (14.5)	13 (23.6)	
FIGO stage			0.421
I	31 (56.4)	35 (63.6)	
II	18 (32.7)	12 (21.8)	
III	6 (10.9)	8 (14.5)	
Histologic grade			0.286
G1	9 (16.4)	12 (21.8)	
G2	29 (52.7)	33 (60.0)	
G3	17 (30.9)	10 (18.2)	
KPS score (points)			0.339
70-80	28 (50.9)	23 (41.8)	
80-90	27 (49.1)	32 (58.2)	

PLD: pelvic lymphadenectomy, PALD: para-aortic lymphadenectomy, FIGO: International Federation of Gynecology and Obstetrics, KPS: Karnofsky performance status.

6 months after radiotherapy and chemotherapy or the presence of new lesions within 1 year after surgery was defined as recurrence. The time from the beginning of randomization to death from any cause was regarded as overall survival (OS).

Statistics

SPSS 22.0 software (IBM, Armonk, NY, USA) was adopted for statistical analyses. Measurement data were expressed by mean ± standard deviation, and t-test was employed for comparison between two groups. Enumeration data were expressed by percentage [n (%)], and comparison between groups was analyzed by x^2. Besides, Kaplan-Meier method was utilized to plot the survival curves, and log-rank test was conducted to determine the presence or absence of statistically significant difference in the survival rate between the two groups of patients. P<0.05 indicated that the difference was statistically significant.

Results

Comparison of surgery between the two groups of patients

The mean operation time was 213.5±32.6 min in the PALD+PLD group, which was significantly longer than 188.9±40.4 min in the PLD group (p<0.001). The amount of intraoperative bleeding was 243.3±82.7 mL and 260.6±80.8 mL in the PLD and PALD+PLD group, respectively, showing no statistically significant difference (p=0.270). In the PALD+PLD group, the average number of resected lymph nodes and the number of positive lymph nodes was 21.1±9.7 and 2.0±4.4, respectively, which was significantly greater than 11.8±6.5 and 0.3±0.9 in the PLD group, revealing statistically significant differences (p<0.001, p=0.006). Besides, there were no statistically significant differences in the volume of postoperative drainage [(585.7±422.9) mL *vs.* (715.9±562.5) mL], postoperative anal exhaust time [(1.9±1.1) d *vs.* (2.1±1.3) d], postoperative catheter indwelling time [(12.4±5.5) d *vs.* (13.4±6.7) d], and postoperative hospitalization time [(14.7±7.8) d *vs.* (16.8±9.0) d] between the two groups (p>0.05) (Table 2).

Incidence of intraoperative and postoperative complications in the two groups

Intraoperative complications mainly included large vessel (including internal iliac vein, common iliac vein and external iliac vein) injury, bladder injury and ureter injury. Postoperative complications mainly involved fever, poor incision healing, lymphatic cyst, urinary retention and ureteral fistula. No statistically significant differences were observed in the incidence rate of intraoperative and postoperative complications between the two

Table 2. Comparison of parameters related to surgery of the studied patients in two different groups

Parameters	*PLD group (n=55)*	*PLD+PALD group (n=55)*	*p value*
Operation time (min)	188.9±40.4	213.5±32.6	0.001
Intraoperative bleeding volume (ml)	243.3±82.7	260.6±80.8	0.270
Number of lymph node dissection	11.8±6.5	21.1±9.7	0.001
Number of positive lymph nodes	0.3±0.9	2.0±4.4	0.006
Postoperative drainage volume (ml)	585.7±422.9	715.9±562.5	0.173
Postoperative gas passage time (d)	1.9±1.1	2.1±1.3	0.386
Catheter indwelling time (d)	12.4±5.5	13.4±6.7	0.394
Postoperative in-hospital time (d)	14.7±7.8	16.8±9.0	0.194
Intraoperative complications, n (%)			0.142
Large blood vessels injury	1 (1.8)	2 (3.6)	
Bladder injury	0 (0)	1 (1.8)	
Ureteral injury	1 (1.8)	3 (5.5)	
Postoperative complications, n (%)			0.138
Fever	4 (7.3)	5 (9.1)	
Poor incision healing	1 (1.8)	3 (5.5)	
Lymphatic cyst	5 (9.1)	7 (12.7)	
Ureteral fistula	1 (1.8)	2 (3.6)	
Intestinal fistula	0 (0)	0 (0)	
Urinary retention	0 (0)	2 (3.6)	
Deep venous thrombosis	1 (1.8)	2 (3.6)	

PLD: pelvic lymphadenectomy, PALD: para-aortic lymphadenectomy.

groups (p>0.05), and there were no serious surgery-related complications or deaths (Table 2).

Follow-up results of tumor recurrence and survival

The total recurrence rate was 9.1% (5/55) *vs.* 20.0% (11/55) between the PLD and PALD+PLD group, showing a statistically significant difference (p=0.045). The postoperative recurrence rate was 6.5% (2/31) *vs.* 2.9% (1/35) in stage I patients and 33.3% (6/18) *vs.* 16.7% (2/12) in stage II patients between the PLD and PALD+PLD group, showing no statistically significant difference (p=0.484, p=0.312). In addition, the recurrence rate of stage III patients was 50.0% (3/6) *vs.* 25.0% (5/55) between the PLD and PALD+PLD group, revealing a statistically significant difference (p=0.034) (Table 3).

All patients were followed up for 22-36 months, with a follow-up rate of 100%. During the follow-up period, the 3-year OS was 90.9% (50/55) and 96.4% (53/55) in the PLD and PALD+PLD group, respectively. The survival curve (Figure 1) was plotted using the Kaplan-Meier method, and no statistically significant difference was observed in the OS between the two groups of patients (p=0.249, log-rank test).

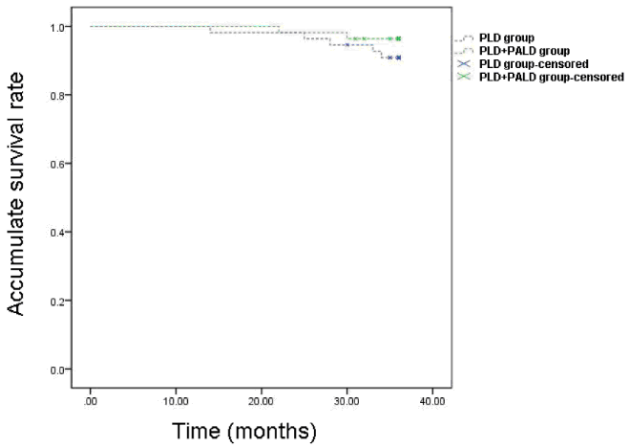

Figure 1. Kaplan-Meier survival curves of patients in the PLD and PLD+PALD group. The difference between overall survival rate of patients in the PLD and PLD+PALD group was not statistically significant (p=0.249).

Discussion

Lymphatic system is a major route of tumor cell dissemination in endometrial carcinoma. According to a report, lymph node metastasis rate in endometrial carcinoma is 5-20%, and lymph node metastasis is the main risk factor for poor prognosis in patients with endometrial carcinoma [6]. Clinically, lymph node resection mainly aims to remove possible metastatic lesions, clarify tumor stage, guide adjuvant therapy, and evaluate and ameliorate the prognosis of patients [7]. However, lymph node resection may induce complications such as vascular and nerve injury, venous thrombosis, lymphatic cyst formation, lymphedema of the lower limbs, and chylous leakage, affecting the patient quality of life [8]. Hence the value and extent of lymph node resection have not yet reached a consensus.

Many gynecologic oncologists in China and foreign countries have conducted a lot of research and discussion on the influence of systemic lymph node dissection on the prognosis of patients since the FIGO staging and standards for endometrial carcinoma were revised in 2009. Some authors pointed out that systemic lymph node dissection can ameliorate the prognosis, but some others considered that pelvic and para-aortic lymphadenectomy does not facilitate the improvement of survival. Kim et al [9] conducted a retrospective review on 786 patients with endometrial carcinoma, and reported that systemic lymph node dissection could ameliorate the prognosis of patients. Alhilli et al [10] also reported that pelvic lymph node dissection could ameliorate the prognosis of patients with medium- and high-risk endometrial carcinoma. However, some other studies have indicated that para-aortic lymphadenectomy for endometrial carcinoma cannot prominently improve the prognosis, and large-scale and excessive dissection will lead to blind expansion of surgical extent, which causes unnecessary damage to the patient, resulting in the occurrence of surgical complications [11,12]. In a previous study, the clinical data of 257 patients with low-risk endometrial carcinoma were

Table 3. Comparison of recurrence rate of the studied patients in two different groups

Parameters	*PLD group (n=55)*	*PLD+PALD group (n=55)*	*p value*
FIGO Stage I	6.5% (2/31)	2.9 % (1/35)	0.484
FIGO StageII	33.3% (6/18)	16.7% (2/12)	0.312
FIGO Stage III	50.0% (3/6)	25.0% (2/8)	0.034
Total	20.0% (11/55)	9.1% (5/55)	0.045

PLD: pelvic lymphadenectomy, PALD: para-aortic lymphadenectomy.

retrospectively reviewed by Turkler et al [13], who reported that there were no statistically significant differences in disease-free survival and OS between those with and without lymph node resection. Eggemann et al [14] conducted a retrospective review on 1.502 patients with endometrial carcinoma, with a median follow-up period of 78 months, to explore the feasibility of lymph node dissection and the effect of resected extent of lymph nodes on the OS, and the results showed that pelvic and para-aortic lymphadenectomy could not ameliorate the OS of patients in low-risk group. However, lymph node dissection could improve the survival of patients in medium-risk group compared with the group without lymph node dissection. In addition, only pelvic and para-aortic lymphadenectomy could notably improve the survival of patients in high-risk group, while pelvic lymph node dissection alone was insufficient. Papathemelis et al [15] reported that for high-grade endometrial carcinoma (type I G3 or type II), the OS and 5-year survival rate in the systemic pelvic and para-aortic lymphadenectomy group (number of resected lymph nodes ≥25) were higher than those in the selective dissection group and non-lymph node dissection group, showing statistically significant differences. Therefore, systemic pelvic and para-aortic lymphadenectomy is recommended for endometrial carcinoma with high-risk factors.

In this study, the operation time was significantly longer in the PALD+PLD group than in the PLD group ($p<0.001$), the average number of resected lymph nodes and the number of positive lymph nodes in the PALD+PLD group were significantly greater than in the PLD group ($p<0.001$, $p=0.006$), and there were no statistically significant differences in other surgery-related indicators between the two groups ($p>0.05$), demonstrating that pelvic and para-aortic lymphadenectomy will extend the patient's operation time to a certain extent, but has no significant impact on the amount of intraoperative bleeding and postoperative recovery. Meanwhile, it can increase the number of resected lymph nodes, which may benefit the prognosis of patients. In addition, no statistically significant difference was observed in the incidence of intraoperative and postoperative complications between the two groups ($p>0.05$), suggesting that pelvic and para-aortic lymphadenectomy will not increase the risk of intraoperative and postoperative complications.

Some studies have pointed out that pelvic lymph node dissection is not an independent influencing factor for the prognosis of patients, and the patient survival rate will not increase due to pelvic dissection. However, most studies have indicated that patients who underwent lymph node dissection have a more prominent long-term effect than those without dissection [16,17]. By comparing the survival of patients with different extents of peritoneal lymph node dissection, it can be seen that pelvic and para-aortic lymphadenectomy can remarkably improve the prognosis of patients with early endometrial carcinoma and high-risk factors, but no statistical difference was found in the prognosis compared with those receiving pelvic lymph node dissection alone [18,19]. For advanced patients, para-aortic lymphadenectomy has a remarkable effect on improving the prognosis, which has been recognized. Para-aortic lymphadenectomy can not only effectively reduce the number of tumor cells in patients with advanced endometrial carcinoma, but also blocks the lymph node metastasis pathway of tumor cells, thus significantly reducing mortality and improving survival [17,20]. According to the follow-up results, the total recurrence rate was 9.1% *vs.* 20.0% between the PLD and PALD+PLD group, showing a statistically significant difference ($p=0.045$). Moreover, the difference in the recurrence rate of stage I and II patients was not statistically significant ($p=0.484$, $p=0.312$), but the recurrence rate of stage III patients between the PLD and PALD+PLD group was significantly different ($p=0.034$). These suggest that para-aortic lymphadenectomy can significantly improve the prognosis of patients at relatively advanced stages, which is consistent with previous reports. During the follow-up period, the 3-year OS was 90.9% and 96.4% in the PLD and PALD+PLD group, respectively, revealing no significant difference ($p=0.249$). The reason may be related to the small sample size enrolled in this study, a certain bias in grouping, a disparity in the proportion of tumor staging, and no consideration about postoperative adjuvant treatment schedules.

This study bears many limitations. For example, the sample size was small, the follow-up time was short, and the follow-up content was not comprehensive enough. Therefore, in the future, large-sample multi-center randomized controlled trials are required to further verify the conclusions of this study.

Conclusions

Laparoscopic pelvic and para-aortic lymphadenectomy for endometrial carcinoma can increase the number of resected lymph nodes and reduce the recurrence rate. Moreover, it does not increase the incidence rate of surgical complications.

Conflict of interests

The authors declare no conflict of interests.

References

1. Polan RM, Rossi EC, Barber EL. Extent of lymphadenectomy and postoperative major complications among women with endometrial cancer treated with minimally invasive surgery. Am J Obstet Gynecol 2019;220:261-3.
2. Zhou L, Guo F, Li D, Qi J, Chan L, Yuan Y. Short- and long-term outcomes of laparoscopic surgery for elderly patients with clinical stage I endometrial cancer. JBUON 2020;25:764-71.
3. Doulgeraki T, Vagios S, Kavoura E et al. Mismatch repair status in high-grade endometrial carcinomas of endometrioid and non-endometrioid type. JBUON 2019;24:2020-7.
4. Lee YC, Lheureux S, Oza AM. Treatment strategies for endometrial cancer: current practice and perspective. Curr Opin Obstet Gynecol 2017;29:47-58.
5. Sari ME, Yalcin I, Sahin H, Meydanli MM, Gungor T. Risk factors for paraaortic lymph node metastasis in endometrial cancer. Int J Clin Oncol 2017;22:937-44.
6. Toptas T, Simsek T, Karaveli S. Prognostic risk factors for lymph node involvement in patients with endometrial cancer. Turk J Obstet Gynecol 2017;14:52-7.
7. Muallem MZ, Sehouli J, Almuheimid J, Richter R, Joukhadar R, Plett H. Risk Factors of Lymph Nodes Metastases by Endometrial Cancer: A Retrospective One-center Study. Anticancer Res 2016;36:4219-25.
8. Todo Y, Okamoto K, Takeshita S, Sudo S, Kato H. A patient group at negligible risk of para-aortic lymph node metastasis in endometrial cancer. Gynecol Oncol 2016;141:155-9.
9. Kim HS, Suh DH, Kim MK, Chung HH, Park NH, Song YS. Systematic lymphadenectomy for survival in patients with endometrial cancer: a meta-analysis. Jpn J Clin Oncol 2012;42:405-12.
10. AlHilli MM, Hopkins MR, Famuyide AO. Endometrial cancer after endometrial ablation: systematic review of medical literature. J Minim Invasive Gynecol 2011;18:393-400.
11. Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 2009;373:125-36.
12. Loubeyre P, Undurraga M, Bodmer A, Petignat P. Non-invasive modalities for predicting lymph node spread in early stage endometrial cancer? Surg Oncol 2011;20:e102-8.
13. Turkler C, Kulhan M, Kulhan NG, Ata N, Sanci M, Ozeren M. Role of lymphadenectomy in disease-free and overall survival on low risk endometrium cancer patients. Ginekol Pol 2018;89:311-5.
14. Eggemann H, Ignatov T, Kaiser K, Burger E, Costa SD, Ignatov A. Survival advantage of lymphadenectomy in endometrial cancer. J Cancer Res Clin Oncol 2016;142:1051-60.
15. Papathemelis T, Scharl S, Kronberger K et al. Survival benefit of pelvic and paraaortic lymphadenectomy in high-grade endometrial carcinoma: a retrospective population-based cohort analysis. J Cancer Res Clin Oncol 2017;143:2555-62.
16. Ignatov A, Ivros S, Bozukova M, Papathemelis T, Ortmann O, Eggemann H. Systematic lymphadenectomy in early stage endometrial cancer. Arch Gynecol Obstet 2020;302:231-9.
17. Bogani G, Dowdy SC, Cliby WA, Ghezzi F, Rossetti D, Mariani A. Role of pelvic and para-aortic lymphadenectomy in endometrial cancer: current evidence. J Obstet Gynaecol Res 2014;40:301-11.
18. Petousis S, Christidis P, Margioula-Siarkou C et al. Combined pelvic and para-aortic is superior to only pelvic lymphadenectomy in intermediate and high-risk endometrial cancer: a systematic review and meta-analysis. Arch Gynecol Obstet 2020;302:249-63.
19. Persson J, Salehi S, Bollino M, Lonnerfors C, Falconer H, Geppert B. Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer (SHREC-trial)-the final step towards a paradigm shift in surgical staging. Eur J Cancer 2019;116:77-85.
20. Kikuchi A, Yanase T, Sasagawa M, Honma S. The role of para-aortic lymphadenectomy in stage IIIC endometrial cancer: A single-institute study. J Obstet Gynaecol 2017;37:510-3.