



Comparison of the Results of Conventional and Laparoscopic Methods of Lymph Node Dissection Performed in Endometrial Cancer Surgery

Endometriyum Kanseri Cerrahisinde Yapılan Lenf Nodu Diseksiyonunun Konvansiyonel ve Laparoskopik Yöntem Sonuçlarının Karşılaştırılması

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ABSTRACT

Objective: The aim of this study was to determine a current approach to en bloc para-aortic lymphadenectomy and to compare the results of this new approach performed by way of laparotomy and endoscopically.

Methods: This study was conducted on 191 patients with endometrial cancer (EC) who had undergone para-aortic lymph node (PaLN) dissection with the current method (en bloc paraaortic lymphadenectomy; protect inferior mesenteric artery and superior hypogastric plexus) between January 2015 and September 2019. A description of the paraaortic lymphadenectomy technique was made in this study. Harvested lymph node counts, operational information, pathological features, postoperative complications, recurrence were presented.

Results: A total of 191 EC patients were analyzed in two separate groups with regard to surgical approach. Open and minimally

ÖZ

Amaç: Çalışmada; en blok paraaortik lenfadenektomiye güncel bir yaklaşım belirlemek ve laparotomi ile endoskopik olarak yapılan bu yeni yaklaşımın sonuçlarının karşılaştırılması amaçlanmıştır.

Yöntemler: Çalışma, Ocak 2015 ile Eylül 2019 tarihleri arasında güncel yöntemle (en blok paraaortik lenfadenektomi; alt mezenterik arteri ve superior hipogastrik pleksusu koruyarak) para-aortik lenf nodu (PaLN) diseksiyonu yapılan 191 endometriyum kanserli (EC) hasta üzerinde gerçekleştirildi. Makalede uygulanan teknik anlatıldı. Alınan lenf nodu sayıları, operasyon bilgileri, patolojik özellikler, postoperatif komplikasyonlar ve nüks oranları belirtildi.

Bulgular: Toplam 191 EC tanılı hasta cerrahi yaklaşım açısından iki ayrı grupta incelendi. Laparotomi grubu ve minimal invaziv cerrahi grubu sırasıyla 141 ve 50 hastadan oluşuyordu. Gruplar arasında yaş, vücut kitle indeksi, menopoz durumu, anestezi süresi,

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Cite this article as: Comba C, Demirayak G, Karakaş S, Erdoğan ŞV, Demir Ö, Yıldız GÖ, Önder AB, Erdoğan A, Afşar S, Özdemir İA. Comparison of the Results of Conventional and Laparoscopic Methods of Lymph Node Dissection Performed in Endometrial Cancer Surgery. *Bezmialem Science*. 2024;12(3):342-9

Received: 23.09.2023

Accepted: 16.04.2024



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ABSTRACT

invasive surgery was composed of 141 and 50 patients, respectively. There was no difference between the groups in respect of age, body mass index, menopausal status, anesthesia time, chylous ascites, the presence of recurrence. We found in open surgery group that pre-operative CA125 level, amount of intraoperative bleeding, erythrocyte suspension transfusion, number of PaLNs, metastatic PaLN counts, and early postoperative complications were significantly higher than the other group.

Conclusion: The current method has some advantages such as protecting normal body structures, resulting in the same lymph node counts with published articles by other authors previously, and having lower recurrence rates. Two approaches of the current technique are feasible, easy to perform and effective.

Keywords: Paraaortic lymphadenectomy, method, endometrial cancer, minimally invasive surgery

ÖZ

şilöz asit, nüks varlığı açısından fark yoktu. Laparotomi grubunda ameliyat öncesi CA125 düzeyi, intraoperatif kanama miktarı, eritrosit süspansiyon transfüzyonu, PaLNs sayısı, metastatik PaLNs sayısı ve erken postoperatif komplikasyonların diğer gruba göre anlamlı derecede yüksek olduğu tespit edildi.

Sonuç: Mevcut yöntemin, normal vücut yapılarını koruması, lenf nodu sayılarının daha önce başka yazarlar tarafından yayınlanan makalelerle benzer olması ve nüks oranlarının daha düşük olması gibi avantajları vardır. Mevcut tekniğin iki yaklaşımı da uygulanabilir, gerçekleştirilmesi kolay ve etkilidir.

Anahtar Sözcükler: Paraaortik lenfadenektomi, metod, endometriyum kanseri, minimal invaziv cerrahi

Introduction

Para-aortic lymph nodes (PaLNs) involvement in tumor cells is important in the stages of gynecologic malignancies including cervical, endometrial, ovarian, and vulvar cancers. Endometrial cancer (EC) is the most common gynecological cancer in the world. Although the sentinel lymph node concept has become widespread in EC surgery in recent times, PaLN dissection is an important part of the surgical procedure (1-3).

The superior hypogastric plexus (SHP) is a preaortic nervous plexus formed by two laterals which originate mainly from the lowest lumbar splanchnic nerves and include a sympathetic component; one median root around the level of aortic bifurcation (4-6). The median root, or a continuation of the abdominal aortic plexus from the inferior mesenteric plexus (4,7), includes both sympathetic and parasympathetic components (8). The SHP is divided into paired hypogastric nerves either at the same level or below the sacral promontory (4,5,7).

The inferior mesenteric artery (IMA) supplies blood to the left side of the colon through the bifurcate left colic artery (LCA) and the sigmoid artery. The frequencies of the bifurcation patterns of the IMA were determined by Muroto et al. (9) in 2015 using three-dimensional computed tomography angiography. The anatomy of the artery and the sparing of it are very important for surgeons and patients who suffer from gynecological cancers or cancers in the left colon segments (9).

The aim of this study was to determine a current approach to en bloc para-aortic lymphadenectomy which would protect the IMA and hypogastric nervous plexus and to compare the results of this new approach performed by way of laparotomy and endoscopically.

Methods

This study was conducted on patients with EC who had undergone PaLN dissection with current methods between

January 2015 and September 2019 with the approval of the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Board (approval Number: 2019/434, date: 30.09.2019). Bakırköy Dr. Sadi Konuk Training and Research Hospital is a center accredited by the European Society of Gynecological Oncology.

Patients who had been diagnosed as having EC and who had undergone a para-aortic lymphadenectomy were included in this study due to the modified Mayo criteria (10).

The study participants were divided into two groups as laparotomy patients (minimally invasive surgery conversion to laparotomy), and those who had undergone minimally invasive surgery (laparoscopy or robotics) according to surgeon's decision. In the groups the same surgical techniques were performed by the same surgical teams.

Informed consent was obtained from patients before the procedure. A statistical program (G*Power version 3 [Heinrich Heine University, Düsseldorf, Germany]) was used to estimate the sample size via a 1-tailed hypothesis using an independent sample t-test with an α error of 0.05 and a power of 0.90. For a moderate effect size ($d=0.50$), a total sample size of 176 was calculated to be required. In the present study, there were 50 women in the minimally invasive group and 141 women in the laparotomy group. Post-hoc analysis for moderate effect size indicated that the power of the test was increased to 0.95. The inclusion criteria for the study were patients who suffered EC and who underwent comprehensive surgical staging with PaLN dissection.

The study exclusion criteria were patients who suffered from another gynecological cancer, synchronous gynecological (ovarian, cervical) or non-gynecological tumors (breast or gastrointestinal tumors), patients who underwent sentinel lymph node dissection without a para-aortic lymphadenectomy, or in whom a pelvic lymphadenectomy only was performed, and those who had undergone a fertility sparing procedure.

Statistical Analysis

SPSS 20 program designed for Windows was used for statistical analysis. All continuous variables were expressed as mean and standard deviation values and categorical variables were expressed as number (n) and percentage of the total group (%). All statistical tests were performed by comparing two groups. Mann-Whitney U test was used for comparative analysis of independent variables and chi-square test was used for categorical variables. A value of $p < 0.05$ was considered statistically significant.

Description of the Surgical Technique

After pelvic lymph node dissection, PaLN dissection begins with an incision to the right pelvic side parietal peritoneum up to the ileocecal region. The right ureter is separated laterally up to the same level. The peritoneum is incised from the medial of the right infundibulopelvic ligament to the inferior mesenteric vein in the open procedure. However, in the minimally invasive procedure, the incision is finished up to 4 cm further from the vessel to tent the peritoneum and to restrain the bowels. The foamy tissues are dissected through the lateral and medial sides up to the ileopsoas muscle and are visible on the right side of the vena cava. The right ureter and right infundibulopelvic ligament are dissected from the medial side up to the level of the right ovarian vein's entrance to the vena cava and the right ovarian vein is then ligated and cut. In general the left renal vein which crosses over the aorta and flows into the vena cava can be visible by dissecting porous tissue and lymphatic veins around the vena cava. Thus the right side is prepared for the lymphadenectomy. Afterwards the incision is enlarged to the pelvic floor from the lateral side of the sigmoid colon to the peritoneum and the ureter is lateralized by way of left ureter dissection. The lymph nodes are dissected through this level with a dissection above the right common iliac artery to isolate the IMA which is located approximately 4 or 5 centimeters above the aorta bifurcation and rises up slightly to the left side. By preserving the superior hypogastric nerves, a passage is carved out between the iliac veins and nerves, ensuring that these nerves remain on the anterior side. The left ureter and left ovarian vein are dissected to the level of the IMA. From that point the lymph nodes are located on the lateral side of the right common iliac artery and the superior and right lateral side of the vena cava are then carefully dissected. It is important to ensure

that the associated veins which are at the level of the iliac artery dissection point and between the vena cava and the lymphatic vessel are intact. Until the level of the IMA para aortocaval lymph nodes is dissected, as the first dissection on the side of the aorta in order to reach the level of the left renal vein, the cranial part is left undissected. Starting from the lateral side of the left common iliac artery, on the medial side the common iliac and the aorta and on the lateral side the psoas muscle are dissected. By preserving the chain, the PaLNs are dissected through the track of the vertebrae to the level of the IMA. Afterwards, in the minimal invasive procedure, the camera is replaced in the suprapubic trocar and the operation is performed from the pelvis to the thorax. First the para aorto-caval lymph nodes, which are left without dissection of its cranial parts, are dissected to the level of the left renal vein and the cranial parts are occluded by using endoclips or suture materials. The PaLNs which are left as a chain to the level of the IMA are dissected a further 1-2 cms and are retracted by crossing over the IMA in order to maintain easier traction on the right side. The superior PaLNs between the aorta and the IMA are harvested as a chain up to the left renal vein cranially and between the aorta and the left ovarian vein. The cranial part is occluded by endoclip or sutures as are the aorto-caval lymph nodes. Afterwards to control hemorrhaging, BLOODCARE powder is applied to the cranial side of the lymph node dissection area. A dissection of presacral lymph nodes is performed with precision starting from the medial side of the right common iliac artery to the left common iliac vein and the middle sacral artery and veins. Thus the PaLN dissection is completed.

Results

A total of 191 patients in accordance with the inclusion criteria of the study were identified in the specified date range and the results were analyzed retrospectively.

These patients were divided into two groups for examination. While the first group was the PaLN dissection using the laparotomy method, the second group was the group undergoing PaLN dissection using minimally invasive surgery (laparoscopy/robotic surgery). The bridge technique described above was used in both groups. The demographic characteristics of the entire population and the groups are shown in Table 1.

Table 1. Demographic characteristics of the all population and individual groups

	All population n=191	Group 1 Open surgery n=141	Group 2 Minimal invasive surgery n=50	p-value
Age	61±8.9 (30-82)	62.8±8.4	58.6±9.7	0.247
BMI	35.5±7.7 (20-68)	36.6±7.4 (20-59)	33.3±7.9 (23-68)	0.578
Menopausal Status	24-premenopause (12.6 %) 167-postmenopause (87.4 %)	14- premenopause (9.9 %) 127- postmenopause (90.1 %)	10- premenopause (20 %) 40- postmenopause (80 %)	0.059
Pre-operative CA125	38.3±90.4 (3-757)	45.8±105.8 (4-757)	19.8±18.3 (3-111)	0.012
Pre-operative CA19-9	17.9±38.7 (1-293)	21.8±45.8 (1-293)	9.5±8.7 (3-40)	0.009

BMI: Body mass index

Table 2. Operation-specific features of the all population and individual groups

	All population n=191	Group 1 Open surgery n=141	Group 2 Minimal invasive surgery n=50	p-value
Type of operation	141- open surgery 50- minimal invasive surgery (laparoscopic / robotic)	137- total abdominal hysterectomy + pelvic + paraaortic lymphadenectomy 4- re-staging surgery (open)	33- laparoscopic hysterectomy + pelvic + paraaortic lymphadenectomy 10- robotic hysterectomy + pelvic + paraaortic lymphadenectomy 5- type B hysterectomy + pelvic + paraaortic lymphadenectomy 2- re-staging surgery (laparoscopic)	
Omentectomy	141 (73.8%) - Present 50 (26.2%) - None	121 (85.8%) - Present 20 (14.2%) - None	20 (40%) - Present 30 (60%) - None	0.000
Operation time (min)	278±71.6 (100-500)	262.9±68.4 (100-470)	320.8±63.1 (180-500)	0.000
Anesthesia time (min)	29.4±9.9 (15-60)	28.5±8.8 (15-50)	32.2±12.3 (15-60)	0.022
Amount of Intraoperative Bleeding (mL)	320.1±265.9 (50-2000)	372.3±282.7 (50-2000)	172.6±125.3 (50-500)	0.000
Pre-operative hemoglobin	12.3±1 (8.3-14.9)	12.3±0.9 (8.3-14.9)	12.3±1.2 (9.2-14.4)	0.877
Post-operative hemoglobin	11.4±0.9 (8.8-14.4)	11.3±0.9 (8.8-14.4)	11.6±1.1 (9-13.2)	0.079
Erythrocyte suspension transfusion	48 (25.1%) - Present 143 (74.9%) - None	44 (31.2%) - Present 97 (68.8%) - None	4 (8%) - Present 46 (92%) - None	0.001
Fresh frozen plasma transfusion	47 (24.6%) - Present 144 (75.4%) - None	43 (30.5%) - Present 98 (69.5%) - None	4 (8%) - Present 46 (92%) - None	0.001
Intraoperative complication	6 (3.1%) - Present 185 (96.9%) None	5 (3.5%) - Present 136 (96.5%) - None	1 (2%) - Present 49 (98%) -None	0.504
Early postoperative complication	27 (14.1%) - Present 164 (85.9%) - None	24 (17%) - Present 117 (83%) - None	3 (6%) - Present 47 (94%) - None	0.039
Type of early postoperative complication	24 - open surgery (24/141) - 17 % 3 - minimal invasive surgery (3/50) - 6%	9 - wound infection 3 - dehiscence 3 - subileus 2 - atelectasis 2 - embolism + wound infection 2 - atelectasis+ wound infection 2 - acute kidney failure 1- obturator nerve injury	2 - wound infection 1 - intraabdominal abscess	
Chylous ascites	17 (8.9%) - Present 174 (91.1%) - None	15 (10.6%) - Present 126 (89.4%) - None	2 (4%) - Present 48 (96%) - None	0.127
Treatment of chylous ascites		5 (33.4%) - Diet 10 (66.6%) - Diet + Total parenteral nutrition	2 (100%) - Diet	

The operations performed in both groups and their features are shown in Table 2. The duration of anesthesia and the duration of the operation were statistically significantly longer in the group that underwent the minimally invasive surgery ($p=0.000$; $p=0.022$, respectively). In addition, the amount of intraoperative bleeding was statistically significantly lower in the group undergoing minimally invasive surgery compared to the group undergoing open surgery ($p=0.000$). The need for erythrocyte suspensions and fresh frozen plasma transfusions was found to be less common in the laparoscopy group ($p=0.001$, 0.001 , respectively). While there was no significant difference between the two groups in terms of intraoperative complication rates, the early postoperative complication rate was statistically significantly higher in the laparotomy group ($p=0.039$).

Among the groups, the number of pelvic and PaLNs and metastatic lymph node numbers collected were statistically significantly higher in favor of open surgery. While the presence of lymphovascular area invasions was more common in the open surgery group ($p=0.045$), there was no difference between the groups in terms of intraabdominal fluid cytology positivity and uterine lower segment involvement ($p=0.973$; $p=0.316$). There was no statistically significant difference between the groups in terms of recurrence rates ($p=0.072$). Pathological outcomes of the cases and their comparisons are summarized in Table 3.

The preoperative and postoperative histological diagnoses, grades and stages of the cases examined are as shown in Figure 1 and Figure 2 (histological grade information of 182 patients

preoperatively was obtained). Having regard to the distribution by stages, the first three rankings in both groups were Stage 1a, Stage 1b and Stage 3c2, respectively.

Discussion

The results of the study which compared two methods for the same operation indicated that the same survival rate, complication-free period, and the recurrence. However, there were some differences including operation times and extent of perioperative blood loss. The both techniques were more practical, successful, effective, and straightforward when compared to conventional techniques.

Systemic para aortic lymphadenectomy is defined as the entire dissection and removal of fat and nodal tissues around the aorta, inferior vena cava, and renal vessels. The dissection level includes the left renal vein cranially and the midpoint of the common iliac vessels caudally (11).

Herd et al. (12) developed a technique based on 100 cases with patients who had undergone a transperitoneal or extraperitoneal approach for PaLN dissection. Dargent et al. (13) described extraperitoneal laparoscopic total PaLN dissection as a two sided approach up to the renal vein in 2000. Lymph node dissection was commenced below the left renal vein. This dissection was performed bluntly, scissors and monopolar and bipolar devices were not commonly used and the lymph nodes were harvested, which placed the left side of the aorta into two separate chains, one of which was the left and ventral surface part, the other was the dorsal part of the aorta (13). However, we demonstrated en

Table 3. Comparative analysis of pathological data of cases

	All population n=191	Group 1 Open surgery n=141	Group 2 Minimal invasive surgery n=50	p-value
Tumor size	3.7±1.8 (0,5-12)	3.9±1.9 (0,5-12)	3.4±1.3 (1-8)	0.062
Number of pelvic lymph nodes	20.5±7.7 (10-70)	21.4±7.9 (10-70)	18±6.1 (10-42)	0.002
Number of paraaortic lymph nodes	18±7.7 (4-46)	19.3±7.8 (7-46)	14.3±6.1 (4-29)	0.000
Total number of lymph nodes	38.6±12.8 (16-93)	40.8±12.9 (21-93)	32.3±9.8 (16-67)	0.000
Metastatic pelvic lymph node count	0.6±1.5 (0-10)	0.7±1.7 (0-10)	0.2±0.6 (0-3)	0.005
Metastatic paraaortic lymph node count	1±3.1 (0-20)	1.2±3.5 (0-20)	0.5±1.6 (0-8)	0.044
Total number of metastatic lymph nodes	1.6±4.5 (0-29)	1.9±5 (0-29)	0.7±2.2 (0-10)	0.018
Intraabdominal fluid cytology	7 (3.7%) - positive 184 (96.3%) - negative	6 (4.3%) - positive 135 (95.7%) - negative	1 (2%) - positive 49 (98%) - negative	0.973
Lymphovascular space invasion	45 (23.6%) - present 146 (76.4%) - none	38 (27%) - present 103 (73%) - none	7 (14%) - present 43 (86%) - none	0.045
Uterine lower segment involvement	41 (21.5%) - present 150 (78.5%) - none	32 (22.7%) - present 109 (77.3%) - none	9 (18 %) - present 41 (82 %) - none	0.316
The presence of recurrence	14 (7.3%) - present 177 (92.7%) - none	13 (9.2%) - present 128 (90.8%) - none	1 (2 %) - present 49 (98 %) - none	0.072
Recurrence area		7 - vaginal cuff 3 - pelvis 1 - abdomen 2 - multiple	1 - vaginal cuff	

with contralateral traction of the lymphatic chain, allowing enhanced vision. Some studies reached the same PaLN counts as our study by way of extraperitoneal PaLN dissection (17).

The current concept of lymph node assessment follows a risk-based algorithm. It suggests a systematic LND in patients with EC and uterine high risk factors. In these patients, the incidence of lymph node involvement is high. Furthermore, in these patients, lymph node metastasis of EC is found to be associated with lymphovascular space involvement (LVSI), non-endometrioid histology, and stage IB (16). In our study, the non-endometrioid histology of EC was higher at 56 (29.32%), LVSI 45 (23.6%), and at higher stages than stage IA 117 (61.25%). Nevertheless, the recurrence rate was significantly lower, it occurred in only 14 patients in total. Approximately 15% of patients with stage I and II EC will suffer a recurrence, this rate in advanced stages and all stages EC is higher than 15% (18,19).

IMA supplies blood to the left part of the colon and divides the sigmoidal (SA) and LCA. The division can occur in four patterns: 1) the LCA arises independently from the SA; 2) the LCA and SA arise from the IMA at the same point; 3) the LCA and SA have a common trunk; 4) there is a deficit of the LCA (20). The level of the IMA at its aortic origin can cause some complications such as bowel anastomosis leakage in patients with colorectal cancer (21). These issues indicate that protection of the IMA during PaLN dissection is very critical to prevent blockage of the blood supply to the left colon segments. Using the current technique, we were able to protect them and to harvest lymph nodes which were placed above the IMA with contra traction of them.

Study Limitations

The hypogastric nerve plays a role in terms of bowel, internal genital organs, and bladder functions. Damage to the fibers may lead to male impotence additionally problems of micturition and defecation were unable to be identified in the female population (4,8). As we were able to protect these structures, we avoided postoperative complications related to these organs and we were able to discharge our patients sooner.

Conclusion

Our particular approach has been evolving since 2015. The authors believe that en bloc lymphadenectomies have increased survival rates and have reduced the recurrence of EC. The protection of the IMA and hypogastric nerve fibers can help to avoid certain postoperative complications.

Ethics

Ethics Committee Approval: This study was conducted on patients with EC who had undergone PaLN dissection with current methods between January 2015 and September 2019 with the approval of the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Board (approval Number: 2019/434, date: 30.09.2019).

Informed Consent: Informed consent was obtained from patients before the procedure.

Authorship Contributions

Surgical and Medical Practices: C.C., G.D., S.K., S.A., İ.A.Ö., Concept: C.C., G.D., Ş.V.E., A.B.Ö., İ.A.Ö., Design: C.C., Ş.V.E., A.B.Ö., İ.A.Ö., Data Collection or Processing: C.C., S.K., Ş.V.E., G.Ö.Y., A.B.Ö., İ.A.Ö., Analysis or Interpretation: C.C., G.D., S.K., Ş.V.E., Ö.D., G.Ö.Y., S.A., İ.A.Ö., Literature Search: C.C., Writing: C.C., Ö.D., A.E., S.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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