

Evaluation of Surgical Lymphadenectomy in Management of Cancer Endometrial

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Abstract

Treatment for most endometrial cancer patients tends to be surgical. The treatment of choice for complete hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy has been an open abdominal approach. The application of pelvic lymphadenectomy in patients with early endometrial cancer is useful because it has a diagnostic role and a therapeutic role, prevents metastasis. It could be concluded that: endometrial cancer surgery can be conducted using an open procedure with high effectiveness in terms of nodal excision and complication rate and increased operational and postoperative enforcement.

Staging endometrial carcinoma to include pelvic lymphadenectomy in the recognition that lymph node status is one of the patients' most important prognostic factors. This led to widespread variations. Pelvic lymphadenectomy allows for accurate prognosis based on a pathological examination of the lymph node. It is an important marker of tumor aggressiveness. Lymphadenectomy distinguishes patients with advanced disease and helps tailor adjuvant therapy for those with adverse risk factors. Thus, it can be concluded that: 1-Pelvic lymphadenectomy has a diagnostic role in the management of adjuvant therapy. Pelvic lymphadenectomy may have a therapeutic benefit, but more studies are needed to confirm this role.

Introduction

Endometrial cancer (EC) is the most common gynecological cancer in developed countries, accounting for about 6 percent of all malignancies [1]. Despite the high prevalence of EC, many of its management features remain unresolved. The most controversial topic of EC treatment is the therapeutic role of lymphadenectomy [2].

The International Gynecology and Obstetrics Federation (FIGO) introduced the concept of EC surgical staging in 1988 and the American College of Obstetricians and Gynecologists (ACOG) approved surgical staging as an important part of EC management in 2005. The ACOG Committee proposed restricting 'adjuvant treatment' to patients with healthy nodes; [3]. Though 'adjuvant radiation therapy is controversial in women with uterine-limited disease based on systemic surgical staging.' Theoretically lymph node removal has several potential benefits. Complete surgical staging can enable the identification of patients with recorded lymphatic dissemination, thereby targeting postoperative care and potentially reducing morbidity [4]. Staging endometrial

carcinoma to include pelvic lymphadenectomy in the recognition that lymph node status is one of the patients' most important prognostic factors [5].

This has contributed to wide variation in practice across the globe. Regional lymphadenectomy is a useful procedure for the purposes of prognosis and staging [6,7] and can potentially provide a significant survival benefit [8].

Some authors however suggested that routine pelvic lymphadenectomy is associated with increased operating time, both intra-and post-operative complications. Lymphadenectomy also adds no However, some authors indicated that routine pelvic lymphadenectomy is associated with increased operating time, complications both intra and post-operative. In fact, lymphadenectomy doesn't bring any advantages to survivors [9].

Aim of the work

The aim of this work was to emphasize the importance of pelvic lymphadenectomy in endometrial cancer management.

Patients and methods

A case series clinical observation study was conducted in the Department of Obstetrics and Gynecology, during the period between February 2018 and August 2019.

This study included 24 patients with clinical stage1 endometrial cancer. All cases underwent total abdominal hysterectomy with pelvic lymphadenectomy.

It should be mentioned that the study in its beginning was designed to include cases with early stages endometrial cancer which was meaning according to FIGO 1988 classification stages I (uterine corpus), and IIA (Endocervical glandular involvement only). These stages became all included in stage I according to FIGO 2009.

Appropriate informed consent was obtained from the patients after a thorough explanation of the planned operation, its potential risks and benefits.

All cases had an established endometrial carcinoma proved by histopathology of the endometrial biopsy. All patients included in this work were subjected to the following:-

- Full history taking
- Examination (general, abdominal, local)
- Investigations:
 1. Routine laboratory investigations as complete blood count, kidney and liver function tests were done.... Etc.
 2. Electrocardiography (ECG) was done.
 3. Ultrasonographic assessment.
 4. Endometrial biopsy & Histopathology was done for every case.
 5. To exclude the suspicion of metastatic disease:

CT scan and / or MRI, Chest X-ray were done.

Preoperative preparation

All the patients underwent the same standard preparation prior to surgery, including antibiotic prophylaxis (Ceftriaxone 1 gm) about half to one hour before operation.

Administration of low molecular weight heparin (LMWH) and compression stockings were applied as prophylaxis against deep vein thrombosis.

Surgical technique

Anaesthesia: All procedures were performed under general anaesthesia with endotracheal intubation.

Position: Patients were positioned supine with sacrum positioned over the table break or over a firm pillow to allow for hyperextension of lumbar spine and better vision into the pelvis.

Incision: Midline vertical incision was the routine approach. The abdomen was kept open by a self-retaining

retractor, and the bowel was kept in place with warm, wet pads. The abdominal viscera were thoroughly examined, including the liver, gallbladder, stomach, and aortic lymph nodes.

a. Pelvic lymphadenectomy

Transperitoneal pelvic lymphadenectomy was initiated. Node. Dissection was started by separating the lymph nodes overlying the outer iliac artery from the vessel by entering the dissection plane between the artery adventitia and the isolar tissue. Dissection was performed caudally down to the inguinal ligament and proximally up to the bifurcation of the iliac. Medially the outer iliac vessels were withdrawn and the dissection was carried between them. The specimen had been removed along the adventitial plane from the medial part of the external iliac artery and vein. Separation of the artery and vein was done to remove the lymph nodes between them. The lymphatic tissue was removed from the outer iliac vein's inferior part. The entire obturator nerve was released from the lymphatic pad with blunt dissection.

Total hysterectomy

After completion of pelvic lymphadenectomy, total hysterectomy was started. The round ligament was cut between two clamps, then the vesico-peritoneal fold was elevated, and the bladder was gently separated from the corpus and cervix and mobilized inferiorly by sharp or blunt dissection. Securing the infundibulopelvic ligament by double ligation was done. Then the uterine arteries were skeletonized, triply clamped, cut and suture ligated. The upper portions of the cardinal ligaments were cut and the uterosacral ligaments were clamped close to the cervix. The vagina was cut free from the cervix and the free edges of the vagina were grasped with long Allis clamps. The vaginal angles were secured with figure-of-eight suture ligatures, and then closure of the vaginal vault was completed.

Results

In the study 24 patients with endometrial cancer were enrolled during the period from February 2018 to August 2019. Both patients experienced total hysterectomy of the uterus with pelvic lymphadenectomy.

For each patient, the following data were collected: age, weight, body mass index (BMI), level, histologic form, tumor grade, operating time, estimated blood loss, perioperative blood transfusions, number and status of lymph nodes obtained, duration of hospital stay, time to restore normal bladder function, intraoperational and postoperative complications.

The results obtained in this work were analysed, tabulated: The patients mean age was 63.5 ± 2.7 years (range from 59 to 68 years). The mean parity was 3.2. And the mean body mass index was 31 ± 4.8 . (T able 1).

AS showed the clinical findings in the studied population. The most common presentation was bleeding which occurred in all patients (100%), followed by diabetes

mellitus in 20 patients and hypertension which occurred in 18 out of 24 patients (83.3%) Table (2).

The laboratory findings in the studied population, the mean hemoglobin concentration was 10 ± 1.6 , the mean white blood cell count was 17.1 ± 4.7 , the mean platelet count was 384.1 ± 228 , the mean alanine aminotransferase was 52.1 ± 25.8 , the mean aspartate aminotransferase was 33.7 ± 8.2 and the mean creatinine concentration was 1.65 ± 0.85 . (Table 3).

Table (4) showed the lymph node status among the studied population. From the 24 patients, 16 patients (66.7%) have positive lymph nodes and 8 patients (33.3%) have negative lymph nodes. The mean diameter was 7.13 ± 1.25 mm.

The mean number of excised pelvic lymph nodes was 15 (ranging from 12-18), The obturator, internal iliac lymph node groups were affected in all patients with positive lymph nodes (16 patients) while external iliac group of lymph nodes was affected in only 4 cases in addition to obturator and internal iliac nodes.

The mean operative time was 140.85 ± 10.1 minutes. The mean amount of blood loss was [127.5 ± 42.9 ml]. The mean number of the pelvic lymph nodes excised was 13.6 ± 3.43 . (Table 4).

Regarding the postoperative details, Hemoglobin decline 24 hours after surgery was (1.52 ± 0.530 gm/dl). Duration of hospital stay was [116.4 ± 17.31 hours]. Complications encountered in this study were: Lymphorrhea in 4 cases. Fever more than 38°C was documented in one case. Blood transfusion was needed for 6 cases. (Table 4 &5).

Histological type, grading, tumor stage is analyzed in table (6). 18 cases were stage IA (75%), 6 cases were stage IB (25%) , 75% of cases proved to be adenocarcinoma , 25% proved to be clear cell carcinoma.

	n = 24
Age (years)	
Mean \pm SD	63.5 ± 2.7
Range	59-68
Parity	
≤ 3	4 (33.3%)
> 3	8 (66.7%)
Body mass index	
Mean \pm SD	31 ± 4.8
Range	24-37

Table 1: Demograohic data of the studied patients.

	No	%
Diabetes mellitus	20	83.3
Hypertension	18	75
Bleeding	24	100

Table 2: Clinical data of studied patients.

	Mean \pm SD (range)
Hemoglobin	10 ± 1.6 (8.1-12.5)
White blood cell count	17.1 ± 4.7 (12-24)
Platelet count	384.1 ± 228 (250-870)
Alanine aminotransferase	52.1 ± 25.8 (18-100)
Aspartate aminotransferase	33.7 ± 8.2 (20-45)
Creatinine concentration	1.65 ± 0.85 (1-3.25)

Table 3: Laboratory investigations of the studied patients.

	n = 24
Diameter (mm)	
Mean \pm SD	7.13 ± 1.25
Range	5.5-8.8
Lymph node	
Negative	4 (33.3%)
Positive	8 (66.7%)

Table 4: Diameter and status of the excised lymph node.

	Mean \pm SD
Operative time (minutes)	140.85 ± 10.1
Blood loss (ml)	127.5 ± 42.9
LN count	13.6 ± 3.4
Intraoperative complications	No
Bowel injury	0
Bladder injury	0
Vascular injury	0
Transfusion	6

Table 5: Operative details of the studied patients.

	No
Hemorrhage	0
Fever	2
Lymphorrhea	4
Postoperative details	Mean \pm SD
Hb% decline (gm/dl)	1.52 ± 0.53
Hospital stay (hour)	116.4 ± 17.31

Table 6: Postoperative complications of the studied patients.

Grade (No.)	No	%
I	6	(25%)
II	12	(50%)
III	6	(25%)
Stage		
IA	18	(75%)
IB	6	(25%)
II	0	0
Histology		
Adenocarcinoma	18	(75%)
Clear cell	6	(25%)

Table 7: Histopathological results in the studied patients.

Discussion

Endometrial carcinoma is one of the most common female genital malignancies, accounting for nearly half of all gynaecologic cancers in united states. About 39,300 new cases are reported annually with over 6,600 deaths. 10 Various early screening methods have been developed for endometrial cancer. Until now, curettage and histological assessment are necessary for definitive diagnosis [2].

Staging endometrial carcinoma to include pelvic lymphadenectomy in the recognition that lymph node status is one of the patients ' most important prognostic factors. This has contributed to wide variation in practice across the globe. Regional lymphadenectomy is a useful treatment for forecasting and staging purposes and may offer a small survival benefit [7].

There is still a general debate in endometrial carcinoma cases management, some add pelvic lymphadenectomy to the radical resection and others deny that role. Therefore, the aim of this work was to develop protocol for the best line in endometrial cancer management.

During the period between February 2018 and August 2019, 24 patients with endometrial cancer were scheduled for total abdominal hysterectomy with pelvic lymphadenectomy at the Department of Obstetrics and Gynecology.

The mean age of the patients in this study was 63.5 ± 2.7 years (range from 59 to 68 years). This was nearly in agreement with reported age incidence for endometrial carcinoma in study done by Lee et al. (2000) who reported that the mean age of endometrial carcinoma at diagnosis is 61 years [11].

.In this study, the most common presentation was bleeding which occurred in all patients (100%), followed by diabetes mellitus and hypertension which occurred in 20 out of 24 patients (83.3%).

This agrees with Soliman et al. (2011) who found that the relative risk of association of endometrial carcinoma with diabetes was 4.1 and with hypertension 1.6, They concluded that diabetics and hypertensives are identifiable

risk group of endometrial carcinomas and thus form a suitable target population for a trial of the efficacy of screening for endometrial carcinoma [12].

In our study, the lymph node status among the studied population. The mean diameter was 7.13 ± 1.25 mm. Obermair et al., (2004) concluded from their study that the positive predictive value of an endometrial thickness greater than 5mm for the presence of cancer was only 35% and it was not possible on the basis of endometrial thickness to descriminate between cases of hyperplasia and carcinoma [18].

Venkat et al., (2011) concluded that It is known that transvaginal sonography has a very high sensitivity to detect early endometrial carcinoma, but the specificity remains low. To order to detect endometrial cancer at an early stage, further tests should be carried out when the endometrial thickness is $> \text{or} = 4$ mm, especially when women have risk factors such as obesity, late menopause or current hormone use [14].

Endometrial thickness greater than 13mm which is hyperechoic or inhomogenous with presence of intratumoral new blood vessels with R.I. < 0.4 were detected in 93.3% of cases of endometrial carcinoma by transvaginal ultrasonography with color flow Doppler with diagnostic accuracy 94.33%, the sensitivity and specificity were 93.33% and 98.33% respectively and P.P.V and N.P.V 93.33% and 98.33% respectively (Kappa = 91.7%) blood flow assessed by color Doppler ultrasound might play an important role in predicting tumor progression and metastasis in endometrial carcinoma [12].

From the 12 patients, 8 patients (66.7%) have positive lymph nodes and 4 patients (33.3%) have negative lymph nodes. This was also suggested by Venkat et al. (2011) [12].

One controversial point is the number of lymph nodes that need to be cut for proper surgical staging. In our study, the mean number of excised pelvic lymph nodes was 15 (ranging from 12-18), this was agreed with Lutman et al. (2006), who found that pelvic lymph node count ~ 12 is an independent prognostic factor for overall and progression-free survival in FIGO stage I and II patients with high-risk histology [13,14].

Chan et al. (2007) and Bijen et al. (2011) Increasing the number of lymph nodes removed and the number of nodal metastases showed a correlation. We concluded that the removal of 21 to 25 nodes was considered to substantially increase the chance of finding at least one metastasis of the lymph nodes [15].

In our study we found that the obturator, internal iliac lymph node groups were affected in all patients with positive lymph nodes (16 patients) while external iliac group of lymph nodes was affected in only 4 cases in addition to obturator and internal iliac nodes.

The routine performance of pelvic lymphadenectomy despite a good portion of study cases can be classified as

low risk for nodal metastasis can be a matter of criticism towards this study. There is a controversy among routine, selective, and no lymphadenectomy for cases of early endometrial cancer. Apparently, it is difficult and ineffective to determine who will and who will not benefit from a lymphadenectomy. Preoperative classification is not representative of postoperative grade with 15 -25% of endometrial cancers with preoperative grade 1 upgraded to final pathology [16,17].

Although lymphadenectomy does not affect survival in this population, it may recognize advanced disease patients and help tailor adjuvant therapy to those with adverse risk factors [18].

In this study, the mean operative time was 140.85 ± 10.1 minutes. It was similar to that reported by Malzoni et al. (2009) [136 ± 3 1min.] and Eisenkop (2010) [139.5 min.]. On the other hand, it was shorter than that reported by Scribner et al. (1999) [237 (185–360) min.], Frigerio et al. (2006) [220 min.] Cho et al. (2007) [154.9 (55–478) min.], Lim et al. (2011) [186.8 ± 59.8 min.] and Soliman et al. (2011) [296.8(230-360) min.] [19,20].

The mean amount of blood loss was 127.5 ± 42.9 ml. This amount of blood loss was reported in a study done by Kondo et al. (2011). As a consequence of reduced blood loss, the mean Hemoglobin decline 24 hours after surgery was 1.52 ± 0.53 gm/dl. This was confirmed by Kondo et al. (2011) [21].

The complications in this study were very limited. There were no cases with hemorrhage. There was one case with fever and two cases with lymphorrhea.

Mariani et al. (2008) reported an institutional algorithm for determining who should undergo lymphadenectomy based on intraoperative grade, distance of invasion, and tumor size [22].

Out of 24 cases, 6 cases were proved to be clear cell carcinoma and 18 cases were proved to be endometrioid type adenocarcinoma, this was in agreement with Venkat et al. (2011) [14].

Conclusion

Pelvic lymphadenectomy plays a diagnostic role in endometrial cancer management.

There may be a therapeutic benefit to pelvic lymphadenectomy but more studies are needed to confirm this role.

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