

ROLE OF PELVIC LYMPHADENECTOMY IN CASES OF GRADE 1 ENDOMETRIAL CANCER

By

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ABSTRACT

Background: Endometrial cancer (EC) is the most common malignancy of the female reproductive tract. Most patients are diagnosed with an early-stage disease, and the overall survival for stage I is about 85–91%.

Objective: To assess the role of pelvic lymphadenectomy in management of early stage endometrial carcinoma in order to determine whether the patient is in need to postoperative radiotherapy or not.

Patients and Methods: This was a prospective observational study included 52 postmenopausal patient who complained from vaginal bleeding and underwent endometrial biopsy revealing the presence of endometrial hyperplasia with atypia or grade 1 endometrial adenocarcinoma attended the Gynecological clinic at Maadi Military Hospital Cairo, Egypt from March 2018 to February 2020.

Results: Myometrial invasion in MRI and histopathology was 73.1% and 65.4% respectively, with no statistically significant difference. Parametrial invasion was 7.7% and 9.6% respectively with no statistically significant difference. Regarding to pelvic nodal invasion in MRI and histopathology, it was 15.4% and 38.5% respectively with a statistically significant difference.

Conclusion: Pelvic lymphadenectomy demonstrated clinical benefit in patients with early stage endometrial cancer and could be a standard treatment option.

Keywords: Endometrial Cancer, Pelvic Lymphadenectomy, Grade 1 endometrial carcinoma.

INTRODUCTION

Endometrial cancer (EC) is the most common malignancy of the female reproductive tract. Most patients are diagnosed with an early-stage disease, and the overall survival for stage I is about 85–91%. Nevertheless, patients with advanced disease and unfavorable pathological characteristics have a guarded prognosis the most significant prognostic factors are histological type and grade, depth of myometrial involvement, lymph vascular invasion, and lymph node (LN) status. 20% of the

patients with EC extending outside of the uterus (stages II and IIIA-B) and 10% of the patients with clinical stage I disease have LN metastases (LNM). Therefore, removal of pelvic and paraaortic LN has been recommended as part of a comprehensive surgical staging including total hysterectomy and bilateral salpingo-oophorectomy (Siegel *et al.*, 2012).

Histologically it constitutes endometrioid adenocarcinomas grade I and II. Endometrial cancer type II is characterized by rapid tumor progression and a biological behavior often similar to

ovarian cancer. Histologically it comprises endometrioid cancer grade 3, and other rare histology, e.g. serous cancers, clear cell cancers and carcinosarcoma, mixed Müllerian tumors (Colombo *et al.*, 2015).

Among patients with LNM, paraaortic LN involvement undoubtedly portends a poorer prognosis and occult paraaortic nodal disease becomes a substantial concern. In a retrospective study, Garg *et al.* (2011) underlined these findings. Among 2559 stage IIIC EC patients, those presenting with paraaortic involvement were more likely to die from their diseases (HR = 1.40 CI). Thus, the FIGO modified its staging of EC and sorted stage IIIC into 2 subgroups according to the paraaortic LN status.

The application of modern imaging tools, like MRI, plays an important role in the preoperative assessment of disease extent and allows the selection of a proper and adequate therapeutic approach for each patient. This way, both the patients requiring a more radical therapeutic approach as well as those who do not require surgery are selected. Internationally, the practice of preoperative MRI evaluation of patients with endometrial cancer differs widely. According to the American College of Radiology (ACR) appropriateness criteria "MRI should be the preferred imaging modality for treatment planning, when available", as it allows best overall assessment of the disease (Lee *et al.*, 2011).

There is increasing evidence that when findings of staging MRI and hysteroscopic biopsy are combined, women at high risk of lymph node metastases can be

identified preoperatively. In one study this yielded an accuracy of 81 % and was superior to combined transvaginal sonography (TVS) and hysteroscopic biopsy (Ortoft *et al.*, 2013).

We aimed in this study to assess the role of pelvic lymphadenectomy in management of early stage endometrial carcinoma in order to determine the patients need to postoperative radiotherapy.

PATIENTS AND METHODS

This was a prospective observational study included 52 patients who attended the Gynecological clinic at Maadi Military Hospital Cairo, Egypt from March 2018 to February 2020.

Inclusion criteria:

Any postmenopausal patient who complained from vaginal bleeding and underwent endometrial biopsy revealing the presence of endometrial hyperplasia with atypia or grade 1 endometrial adenocarcinoma.

Exclusion criteria:

1. Other pelvic tumors.
2. Advanced endometrial cancer.
3. Recurrent endometrial carcinoma.
4. Any types of lymphomas or leukemia.
5. Secondary uterine cancer.

All women in the study were subjected to the written consents, full history taking, physical examination and magnetic resonance imaging (MRI) to detect myometrial invasion, parametrial invasion and pelvic nodal invasion.

Staging of the endometrial cancer was according to FIGO 2009 criteria had been done.

All patients underwent laparotomy for total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), and pelvic lymphadenectomy. Specimen had been examined at the Pathology Department at Maadi Military Hospital to assess the uterus, ovaries and lymph nodes (LNs).

Approvals of the ethical committee, patients were properly counseled as regards the type, methodology and value of study.

Statistical analysis:

Data were collected throughout history, basic clinical examination; laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. The data

collected were tabulated and analyzed by SPSS (statistical package for the social sciences) version 25 (Armonk, NY: The IBM Corp) on IBM compatible computer. Two types of statistics were done:

- According to the type of data; qualitative data were represented as number and percentage, while quantitative continuous data were represented by mean ± SD.
- Chi-square test (χ^2) was used for comparison and association between two qualitative variables.
- A P-value of ≤ 0.05 was considered statistically significant.

RESULTS

Our results showed that the range of age of studied patients 46-75 year and mean ± SD of BMI of patients was 33.1 kg/m² ±4.9. As regards parity, 7.6% was nulliparous, 3.8% primiparous and 84.6% multiparous. Also, 53.8% of patients have

hypertension, 28.8% have Diabetes Mellitus and 5.7% have hypothyroidism.

The tumor was located in the endometrium in 41 patients, fundal region in 8 patients, lower uterine segment in 2, and metastatic tumor in the ovary in 1 patient (Table 1).

Table (1): Site of tumor in studied patients

Sites	Cases	No	(%)
Endometrium		41	(78.8%)
Fundal		8	(15.5%)
Lower uterine segment		2	(3.8%)
Ovarian metastasis		1	(1.9%)

Table 2, shows that MI in MRI and histopathology was 73.1% and 65.4%

respectively with no statistically significant difference; parametrial

invasion was 7.7% and 9.6% respectively with no statistically significant difference. Regarding to pelvic nodal invasion in MRI and histopathology, it was 15.4%

and 38.5% respectively with a statistically significant difference (p- value=0.001- **Table 2**).

Table (2): Comparison between MRI and histopathology results

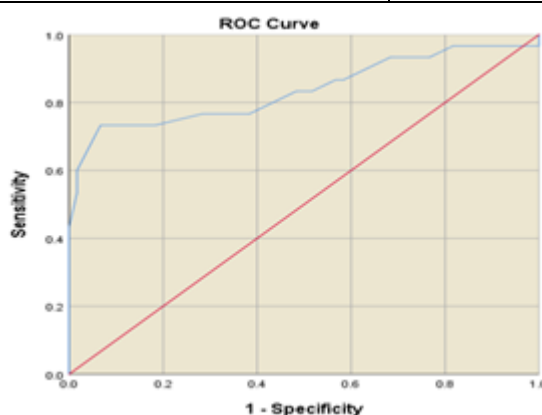
Parameters Sites	MRI (n=52)	Pathology (n=52)	P- value
Myometrial invasion			
- Less than 50%	38 (73.1%)	34 (65.4%)	>0.05
- More than 50%	9 (17.3%)	13 (25%)	
Parametrial invasion	4 (7.7%)	5 (9.6%)	>0.05
Pelvic nodal invasion	8 (15.4%)	20 (38.5%)	0.001

As regard to postoperative complication, excessive drain output was 9.6%, paralytic- ileus 1.9%, wound

Infection was 3.8%, Urinary incontinence 1.9% and incisional hernia was 1.9% (see **Table 3**).

Table (3):Postoperative complication in studied patients

Complications	Cases	No (%)
Excessive drain output		5 (9.6%)
Paralytic ileus		1 (1.9%)
Wound Infection		3 (3.8%)
Urinary incontinence		1 (1.9%)
Incisional hernia		1 (1.9%)



Receiver operating curve (ROC) showed that sensitivity of MRI for detecting pelvic nodal invasion was 78.5%, specificity 73.3%, positive

predictive value 69.4%, negative predictive value 75% and AUC was 0.836 (**Figure 1**).

Figure (1): ROC curve of Pelvic nodal invasion by MRI

DISCUSSION

Lymphadenectomy is widely used to assess whether endometrial cancer has metastasized and reduces the risk of lymphatic metastasis. Non-systematic lymphadenectomy usually involves removing <11 lymph nodes. However, to try to treat and prevent metastases, physicians often perform systematic lymphadenectomy, which involves removing ≥ 11 lymph nodes in the same area covered by non-systematic lymphadenectomy. Systematic lymphadenectomy is significantly more invasive than the non-systematic procedure, and leaves patients with markedly lower postoperative lymph function, increasing the risk of various complications (*Zhang et al., 2012*).

Theoretically, the removal of lymph nodes has several potential advantages. Complete surgical staging may allow the identification of patients with documented lymphatic dissemination, thus targeting postoperative treatment and potentially reducing the morbidity related to unnecessary radiation therapy. Moreover, lymph node dissection may eradicate metastatic lymphatic disease (*Bogani et al., 2014*).

In the present study, 88.5% of patient's preoperative histology of D& C biopsy was endometrioid, 7.7% was complex atypical hyperplasia, 1.9% was scanty tissue and 1.9% was necrotic tissue.

This was in agreement with the study of *Bogani et al. (2014)* in which 81% of patient's preoperative histology of D& C biopsy was endometrioid, and 19% were non-endometrioid. Also, *Abd El-Wahed et al. (2017)* reported in his study that as regard histological data, type I

endometrial carcinoma comprised 27 cases of endometrioid adenocarcinoma, six cases of endometrioid carcinoma with squamous differentiation, 15 cases of villoglandular variant of endometrioid carcinoma, and only one case of mucinous adenocarcinoma. Type II endometrial carcinoma comprised six cases of papillary serous adenocarcinoma, six cases of clear cell carcinoma, and six cases of grade III endometrioid carcinoma.

On the other hand, in the present study, we evaluated MRI of patients preoperatively, and found that 73.1% have myometrial invasion of less than 50%, 17.3% have MI of more than 50%, 7.7% have parametrial invasion and 15.4% have pelvic nodal invasion.

In agreement with our study, the study of *Bogani et al. (2014)* revealed that 77% have myometrial invasion of less than 50%, 23% have MI of more than 50%. Also, our findings were supported by the study of *Rahmani et al. (2018)*, in which histopathological evaluation showed that 64.4% of patients had less than 50% myometrial invasion (superficial myometrial invasion, SMI) and 35.6% had more than 50% myometrial invasion (deep myometrial invasion, DMI).

In addition to above findings, in the present study as regard comparison between MRI and histopathology results, we found that MI in MRI and histopathology was 73.1% and 65.4% respectively with no statistically significant difference. Parametrial invasion was 7.7% and 9.6% respectively with no statistically significant difference. Regarding to pelvic nodal invasion in MRI and histopathology, it was 15.4%

and 38.5% respectively with high statistically significant difference

As regard receiver operating characteristics of pelvic nodal invasion by MRI, we found that sensitivity of MRI for detecting pelvic nodal invasion was 78.5%, specificity 73.3%, positive predictive value 69.4%, negative predictive value 75% and AUC was 0.836. The sensitivity for evaluating lymph node metastasis using MR was not high, as MR was capable of finding lymph node metastasis only when nodes were swollen (>10 mm).

CONCLUSION

Pelvic lymphadenectomy demonstrated clinical benefit in patients with early stage endometrial cancer and could be a standard treatment option.

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دراسة دور استئصال الغدد الليمفاوية الحوضية في حالات المرحلة المبكرة لسرطان بطانة الرحم

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خلفية البحث: سرطان بطانة الرحم هو أكثر أنواع الأورام الخبيثة شيوعاً في الجهاز التناسلي للإناث. يتم تشخيص معظم المرضى بالمرض في مرحلة مبكرة، ويبلغ معدل البقاء على قيد الحياة للمرحلة الأولى حوالي 85-91%.

الهدف من البحث: تقييم دور استئصال الغدد الليمفاوية في الحوض في إدارة المرحلة المبكرة من سرطان بطانة الرحم من أجل تحديد الحاجة إلى العلاج الإشعاعي بعد الجراحة.

المرضى وطرق البحث: تضمنت دراسة رصدية مستقبلية لـ 52 مريضة في مرحلة ما بعد الطمث اشتهن من نزيه مهلبى، وخضعن لخزعة بطانة الرحم كاشفة عن وجود فرط تنسج بطانة الرحم مع اللانمطية أو سرطان غدد بطانة الرحم من الدرجة الأولى الذين حضروا عيادة أمراض النساء في مستشفى المعادي العسكري بالقاهرة خلال الفترة من مارس 2018 إلى فبراير 2020.

نتائج البحث: كان غزو عضل الرحم في التصوير بالرنين المغناطيسي والتشريح المرضى 73.1%، و65.4% على التوالي مع عدم وجود فرق معتد به إحصائياً، وكان الغزو بما يحيط بالرحم 7.7%، و9.6% على التوالي مع عدم وجود فرق يعتد به إحصائياً. وفيما يتعلق بالغزو العقدي للحوض في التصوير بالرنين المغناطيسي ونتيجة تشريح العينة، فقد كان 15.4%، و38.5% على التوالي مع وجود فرق ذو دلالة إحصائية عالية (p-value = 0.001).

الاستنتاج: استئصال العقد اللمفية له فائدة للمريضات اللاتي يعانين من سرطان بطانة الرحم في مراحلها المبكرة، وبالتالي ينبغي أن يكون خياراً علاجياً قياسياً.