Suez Canal University Medical Journal Vol. 26 (1), 2023
Pages 70-75

Evaluation of Sentinel Lymph Node Mapping in Uterine Cancer Staging

Hamada Fathy, Mahmoud G. Hussin*, Ahmed AboBakr, Solimam El-Kammash, Ahmed M. Gomaa

Department of Surgery, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Abstract

Background: **Lymphatic mapping recently emerged as a promising new strategy and is increasingly being adopted by gynecologic oncology practices worldwide. The sentinel lymph node is a technique used to properly detect nodal metastases hence improving staging accuracy with the subsequent proper application of adjuvant therapy.** ***Aim:*** **to evaluate of the accuracy of sentinel lymph node biopsy using a patant blue dye in endometrial and cervical malignancies.** ***Patients and Methods:*** **Twenty-six patients, diagnosed with endometrial cancers stage (I/II) by MRI, and three patients, diagnosed with cervical cancers stage (Ia/IIa) by MRI, were enrolled in the study.** ***Results:*** **Sentinel lymph node(s) were successfully identified in 18 patients (69.2%) with endometrial carcinoma and one case with cancer cervix. The sensitivity of sentinel Lymph node mapping in the detection of lymph node metastasis was 100% with a negative predictive value of 100% and 0% false negative rate. There was a statistically significant inverse relation between sentinel lymph node detection and tumor grading. There was a statistically significant relation between sentinel lymph node detection and both cervical involvement and positive lymph node metastasis.** ***Conclusion:*** **Sentinel Lymph node mapping in cases of early-stage endometrial cancer is a good option to avoid overtreatment with unnecessary removal of more lymph nodes, which may result in an increase in perioperative adverse effects.**

Keywords: Sentinel Lymph Node, Lymphatic Mapping, Endometrial Carcinoma, Cancer cervix

Introduction

Uterine cancer is one of the top-ranking cancers in women with wide international variations in incidence rates. Developed countries have higher incidence rates than developing countries. Egypt has a significantly lower incidence of uterine cancer than other countries in the Middle East. The incidence rate of uterine cancer in Egypt, which increased significantly over the last 12-year period, is around 4.1 per 100000 compared to 8.2 per 100000 which is the global incidence rate[1]. Endometrial cancer arises from the inner layer (endometrium) of the uterus, the origin of approximately 90% of uterine cancers, followed by uterine sarcoma that arises from the outer layer (myometrium) (8%) and less frequent types of cancer (2%)[2]. Uterine carcinoma staging allows appropriate treatment options to be considered and enables greater prognostic accuracy for uterine carcinoma. Staging

*Corresponding Author: mgmhussin@gmail.com

can be based on the TNM or The International Federation of Gynecology and Obstetrics (FIGO) system. MR imaging is the modality of choice for staging both endometrial and cervical carcinoma with CT having relatively low specificity, especially for myometrial invasion[3]. Sentinel lymph node biopsy (SLNB) involves removing a sentinel or watchman lymph node, the first node involved in the movement of a tumor from primary cancer to the lymph nodes. If this is negative, it is surmised that the other nodes are not involved[4]. It is likely that sentinel nodal status could influence the administration of adjuvant therapies such as radiation, chemotherapy, or both. Among the gynecological cancers, SLNB could make a significant impact on women with endometrial cancer. A variety of methods have been described to detect a sentinel node in situ including colored dyes and radioisotopes, the latter requires a specialized gamma detection probe[5]. The rationale of this study is to assess sentinel lymph node mapping among patients with endometrial and cervical cancers. The objective of this study is to evaluate the detection rate of sentinel lymph nodes after sub-serosal injection of patent blue in endometrial and cervical cancer patients.

Patients and Methods

This analytic cross-sectional study was conducted on patients with endometrial cancer and cancer cervix in the Department of Surgery, Suez Canal University Hospital, Ismailia, Egypt in the period between March 2019 and September 2021. The study protocol was revised and approved by the local ethical committee of the faculty of medicine and informed consent was obtained from each patient. Patients diagnosed with endometrial cancers stage (I/II) by MRI and those diagnosed with cervical cancers stage (Ia/IIa) by MRI were enrolled in the study. Excluded from the study were patients who were unfit for surgery and patients with uterine cancer other than endometrial or cervical cancer. All included patients were subjected to detailed medical history, full general examination, and thorough abdominal examination. Liver function tests, CA125, chest radiograph, Pelviabdominal US, and pelvic MRI were performed to exclude distant metastasis.

Intraoperative

Once the patient was under anesthesia, an exploratory laparotomy is performed, and the tumor was identified. The peritoneum over pelvic spaces was mobilized carefully. Then, lymphatic mapping was performed using 1–2 ml of isosulfan blue dye (Patent Blue, 2.5% Guerbet laboratories, France). The dye was injected sequentially into the sub-serosa of the uterus (Figure 1).

SLN mapping

After a few minutes (5-10 min), the pelvic spaces were examined for blue-stained LNs (Figures 2 & 3). The primary tumor and its draining lymphatic basin containing the non-SLNs were processed histologically in the standard fashion with H&E staining. Each SLN was cut into sections and stained with H&E.

Statistical Analysis

Data from history, operative findings, and pathological assessment of SLNs and non-SLNs (after H&E staining) were analyzed by statistical package for social science SPSS 20 (SPSS Inc., Chicago, IL, USA). Quantitative data are expressed as mean and standard deviation while qualitative data are expressed as numbers and percentages of the total.

Results

The study included 26 patients with early-stage endometrial cancer and 3 patients with early-stage cervical cancer. Regarding Endometrial Cancer Cases: Age of the studied patients ranged between 46 to 80 years (mean 62.47±8.43). BMI ranged between 25 to 42 (mean 34.16 kg/m^2). Some of the studied patients had hypertension 46.2% while diabetes accounted for 26.9% of the studied patients.

Table 1: Pathological types and tumor grades of endometrial cancer patients based on preoperative biopsy

	Number (N=26)	Percent
Type		
Endometrioid	23	88.5
Mixed	1	3.8
Serous	2	7.7
Grade		
I	19	73.1
II	6	23.1
III	1	3.8

Table 2: Pathological findings of the final specimen of endometrial cancer patients

	N=26	%
Grade		
I	16	61.5
II	8	30.7
III	2	7.7
Type		
Endometrioid	23	88.5
Serous	1	3.8
Mixed Mullerien	2	7.7
Myometrial involvement:		
No or < 50%	18	69.2
> 50%	8	30.8
Cervical involvement	2	7.7
Adnexal involvement distant metastasis	1	3.8
Disease stage		
I-II	23	88.5
III-IV	3	11.5
LN metastasis:	3	11.5

About 19.2% of patients had more than one comorbid disease. The pathological examination of the preoperative specimen revealed a higher prevalence of the endometrioid type 88.5% and grade I tumor 73.1%. Thirty-eight and a half percent of the studied patients had thickened endometrium (without well-defined mass). Endometrial thickness ranged between 7 to 32 mm with a mean of 18.27 mm. On the other hand, 61.5% of the patients had well-defined intra-luminal mass. The tu-

mor's diameter ranged between 4 to 92 mm with a median of 51.0 mm and a mean of 50.13 ± 20.98. More than half of the studied patients had grade I tumor. Endometrioid type is predominant at 88.5%. About 69% of them had myometrial invasion less than 50%. Eleven and a half percent had lymph node involvement. The number of excised LNs ranged from 7 to 24 with a median of 12. SLNs were detected in eighteen patients. Among patients with detected SLNs, the number of sentinel lymph nodes ranged between 1 to 5 with a median of 3. Of them, 44.4% were detected in the obturator LNs' region. The sensitivity, as well as the specificity of SLN mapping in the detection of lymph node metastasis in endometrial cancer patients, was 100% with a negative predictive value of 100% and 0% false negative rate. Regarding cancer cervix cases, Two cases were squamous cell carcinoma and large cell non-keratinizing. The third one was cervical adenocarcinoma. Only one case (squamous cell carcinoma) showed a stained obturator sentinel lymph node.

Table 3: The detection rate of SLNs and the site of detected LNs in endometrial cancer patients (n=26)

	Patients with detected SLNs (N=18)	Percent
Site of detected SLNs		
Obturator	8	44.4
Internal iliac	4	22.2
External iliac	6	33.3

NB: Patients with detected SLNs are 18/26 (69.2)

Discussion

Our study included 26 patients with early-stage endometrial cancer patients and 3 patients with early-stage cervical cancer. Sentinel lymph node mapping was done using patent blue dye. Most studied patients in the current study had grade I tumors (61.5%) with a predominance of endometrioid type (88.5%) followed by serous and mixed mullerian types. Safta et al[4] reported discordance of the grade in 28.4% of patients with 22.4% underestimated and 6% overestimated. Le and his group also found higher final tumor grade in 22.6% of patients and a change of the histologic type to non-endometroid type was found in 5.3% of patients[4-5]. In the current study, most cases were diagnosed to have stage I disease (22 cases). The high prevalence of early-stage endometrial cancer in the current study is justified by the exclusive selection of early-stage disease, diagnosed based on clinical and imaging findings, to be enrolled in the study. However, upstaging that occurred in 3 cases (11.5%) means that preoperative workup can't accurately detect the disease stage. Surgical staging is mandatory. Eighteen out of the 26 patients with early-stage endometrial cancer, who were included in the current study, had their lymph nodes stained yielding a detection rate of 69.2%. Comparing the current results with other studies, Eitan et al.[6] performed robotic surgical staging, which yielded an overall detection rate of 62.1%. Approximate overall detection rates were reported by another two studies. One performed staging laparotomy (61% detection rate). The other study performed laparoscopic and robotic surgical staging (64.4% detection rate). Higher detection rates were reported in another two studies.

One of them was performed by laparoscopy (overall detection rate of 83%). The other one was performed by robot-assisted surgery (overall detection rate of 75%). Higher detection rates in laparoscopic and robot-assisted surgery compared to our study (69.2%) were justified by the rapid access to pelvic spaces and wide and magnified view[7-11]. In the current study, the number of sentinel lymph nodes detected in patients with successful mapping ranged between 1 to 5 (median 3 lymph nodes per case). An approximate SLN count was reported by Ehrisman et al.[12] who reported a median number of sentinel lymph nodes as 2 per case (range, 0-7). Another recent study reported the median SLN count as one per case (range, 1-3)[13]. Regarding cervical cancer patients in the current study, unfortunately, only three patients met the inclusion criteria. The majority of cervical cancer patients were presented in the advanced stage due to the non-availability of the national screening program.

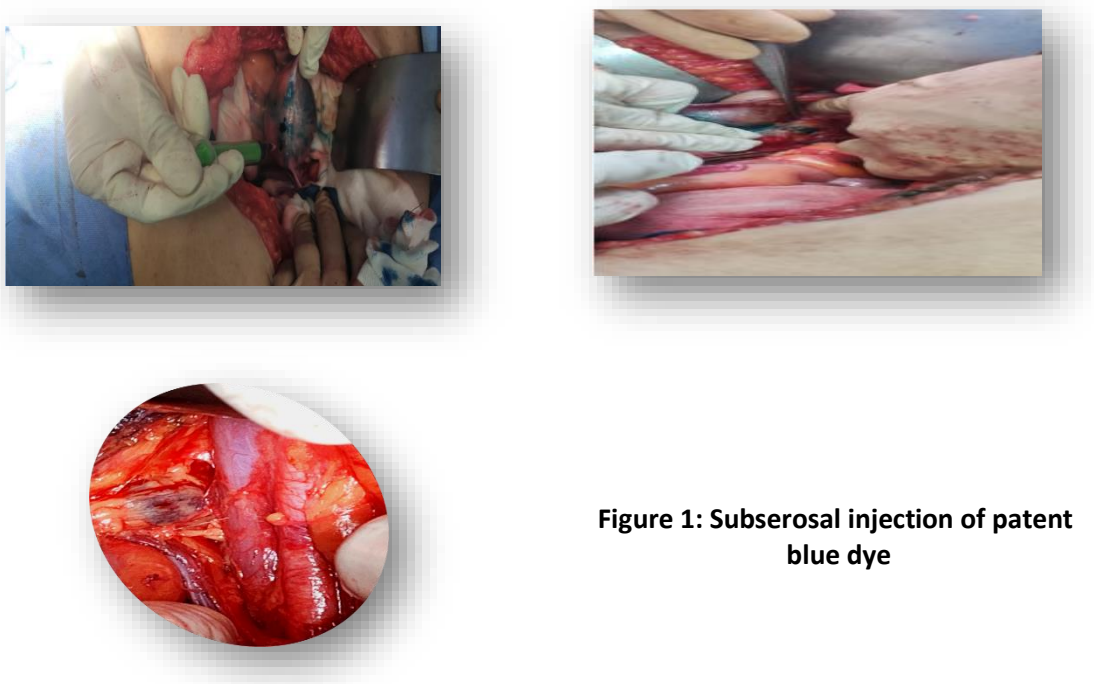

Figure 1: Subserosal injection of patent blue dye

Conclusion

Sentinel lymph node detection could be a promising substitution for the classic pelvic lymphadenectomy in the management of endometrial cancer.

Acknowledgment
Special thanks, admiration, and respect to all radiology members for their kind help, guidance, and valuable support.

References

1. Alshahrani S, Soliman A, Hablas A, et al. 2018. Changes in Uterine Cancer Incidence Rates in Egypt. Obstet Gynecol Int., 2018, pp.1-10.
2. Abu-Rustum N. 2013. Update on sentinel node mapping in uterine cancer: 10-year experience at Memorial Sloan-Kettering Cancer Center. J. Obstet. Gynaecol. Res., 40(2), pp.327-334.
3. Abu-Rustum N, Iasonos A, Zhou Q, et al. 2008. Is there a therapeutic impact to regional lymphadenectomy in the surgical treatment of endometrial carcinoma? AJOG, 198(4), pp.457.e1-457.e6.

4. Cox Bauer C, Greer D, Kram J, et al. 2016. Tumor diameter as a predictor of lymphatic dissemination in endometrioid endometrial cancer. Gynecol. Oncol., 141(2), pp.199-205.
5. Safta I, Jaidane O, Mansouri H, et al. 2018. Survival and prognostic factors of lymphadenectomy in endometrial cancer: a Tunisian single center experience. Int. Surg. J., 5(11), p.3658.
6. Le T, McDonald S, Samant R, et al. 2019. Robotic sentinel node mapping in clinical stage 1 endometrial cancer using methylene blue dyes using the robotic platform. Int J Med Robot., 15(4).
7. Eitan R, Sabah G, Krissi H, Raban O, et al. 2015. Robotic blue-dye sentinel lymph node detection for endometrial cancer – Factors predicting successful mapping. EJSO, 41(12), pp.1659-1663.
8. Lee S, and Atri M, 2019. 2018 FIGO Staging System for Uterine Cervical Cancer: Enter Cross-sectional Imaging. Radiology, 292(1), pp.15-24.
9. Sinno A, Fader A, Roche K, et al. 2014. A comparison of colorimetric versus fluorometric sentinel lymph node mapping during robotic surgery for endometrial cancer. Gynecol. Oncol., 134(2), pp.281-286.
10. Tanner E, Sinno A, Stone R, et al. 2015. Factors associated with successful bilateral sentinel lymph node mapping in endometrial cancer. Gynecol. Oncol., 138(3), pp.542-547.
11. Todo Y, Kato H, Kaneuchi M, et al. 2010. Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis. The Lancet, 375(9721), pp.1165-1172.
12. Ehrisman J, Secord A, Berchuck A, et al. 2016. Performance of sentinel lymph node biopsy in high-risk endometrial cancer. Gynecol. Oncol. Rep., 17, pp.69-71.
13. Weiss L, and Schmid-Schönbein G, 1989. Biomechanical interactions of cancer cells with the microvasculature during metastasis. Cell Biochem. Biophys. , 14(2), pp.187-215.