The Journal of Obstetrics and Gynecology of India (July–August 2022) 72 (S1):S243–S247
https://doi.org/10.1007/s13224-021-01509-7

ORIGINAL ARTICLE

A Study on the Detection Rates and Location of Sentinel Lymph Node in Patients with Gynecologic Cancers

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Received: 18 October 2020 / Accepted: 24 May 2021 / Published online: 6 August 2021

Abstract

Introduction Sentinel lymph node mapping is emerging as an accurate technique to assess the lymph nodal status while reducing surgical and postoperative morbidity. Present study looks into the detection rates and location of sentinel nodes during Sentinel node mapping when Indocyanine green dye was used as a tracer.

Methods This is a single institutional study with details retrieved from a prospectively maintained database. All patients who underwent sentinel node mapping using ICG dye for atypical hyperplasia, endometrial and cervical cancers from February 2015 to April 2020 were included. Location of the sentinel node was taken from the graphical record maintained during surgery. The data obtained are expressed as number and percentage and/or mean and standard deviation for continuous variables. Chi-square test was performed to compare categorical variables.

Results Two hundred and seventy-nine patients underwent sentinel node mapping with ICG dye during this period. Mapping was successful in 270 patients (96.8%) with 85% having successful bilateral mapping. Obturator was the most common location (52%) followed by external iliac (34%). There was no significant difference in detection among patients with BMI less than 30 or more than 30. The detection rate across various histologies of endometrial cancer was also similar.

Conclusion Sentinel node mapping using ICG dye has got excellent overall and bilateral detection rates making it a valuable tool. Obturator was found to be the most common location for the sentinel node. Mapping using ICG dye yield good detection rates in all histologies of endometrial cancer and in patients with high BMI.

Keywords Sentinel lymph node · Endometrial cancer · Cervical cancer · Indocyanine green dye

Introduction

Lymph node status is one of the most important prognostic factors in endometrial carcinoma [1] and since last year the new FIGO staging has incorporated nodal status as a part of cervical cancer staging [2]. Sentinel lymph node mapping (SLNM) is gaining more acceptance in the management of endometrial and cervical cancers [3, 4]. Besides providing accurate information about the nodal status, SLNM reduces the needs for extensive nodal dissection, thus reducing surgical and postoperative morbidity [5].

The technique of sentinel node mapping involves identifying the first node or the sentinel node of that organ. This involves injecting a dye or radioactive tracer into the organ and tracing the lymphatic pathway visually or using a gamma probe in case of radioactive tracer like Technitium-99. Among the methods using blue dye, Indocyanine green (ICG) dye or technitium-99, use of ICG was shown to be accurate in identifying the sentinel node [6, 7].

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With the use of sentinel node mapping, it was seen that the site of sentinel node varied from the usual obturator and iliac locations to the less common para-aortic and pre-sacral locations [5, 8]. This study looks into the sentinel node locations when sentinel node mapping using ICG dye was used for endometrial and cervical cancers and also the detection rates across different groups of patients.

Methods

This is a single institutional study with information retrieved from a prospectively maintained database. All patients who underwent sentinel node mapping using ICG dye for atypical hyperplasias, endometrial and cervical cancers from February 2015 to April 2020 were included. Endometrial cancer patients underwent sentinel node mapping only if they had clinically and radiologically uterus confined disease. Cervical cancer patients were selected for surgery only on they had less than 2 cm tumor with no evidence of parametrial invasion or enlarged lymph nodes on magnetic resonance imaging. Patients who had undergone previous pelvic radiation, retroperitoneal surgery, chemotherapy for endometrial or cervical cancer did not undergo sentinel node mapping.

ICG dye available as 25 mg powder was diluted to a concentration of 0.5% for injection. All patients with atypical hyperplasia and endometrial cancer received the injection at 3 O clock and 9 O clock position both superficially and deep into the cervix. Cervical cancer patients received the injection peritumorally. The injection was done after placing the robotic surgical ports and Docking of the robotic system was done after the injection. The fluorescence was detected with the near infrared (NIR) imaging system of daVinci Xi robotic camera.

Sentinel node mapping was noted as successful when fluorescent lymphatics were visible draining from the site of injection toward sentinel nodes in pelvis or para-aortic area. Special efforts were made to trace the lymphatic from the site of injection to identify the correct sentinel node. A node was marked as a sentinel node only when direct lymphatic channels were seen draining to the node from the site of injection. When the efferent lymphatics were seen going from the sentinel node to another node which was fluorescent, that node when removed, was marked as second in line node.

The identified sentinel nodes were removed and sent for histopathologic examination. Frozen section was done only for patients undergoing sentinel node mapping for cervical cancer. Sentinel node mapping algorithm [9] was followed and any enlarged lymph nodes were removed in addition to the sentinel node. The location of sentinel nodes was marked graphically. Some patients had more than one channel on a side leading to more than one sentinel node locations, and these were also noted as additional sentinel sites. These nodes were removed and labeled as second true sentinel node. Fluorescent lymphatic channels leading to second draining nodes from sentinel sites were noted, but these nodes when removed were marked as second in chain nodes and not as sentinel node.

SLN detection rate was defined as the proportion of patients in whom at least one sentinel node was identified during SLN mapping. The data obtained are expressed as number and percentage and/or mean and standard deviation for continuous variables. Chi-square test was performed to compare categorical variables. p value less than 0.05 was defined as statistical significance for all comparisons. Statistical analysis was done with IBM SPSS v.20 (IBM Corp. NY, USA).

Results

Two hundred and seventy-nine patients underwent sentinel node mapping with ICG dye during this period. Most of the patients had endometrial cancer (200, 71.6%), followed by atypical hyperplasia endometrium (47, 16.8%). Clinicopathologic details are given in Table 1. Mapping was successful in 270 patients (96.8%) with 85% having successful bilateral mapping. Twenty-four patients had more than one lymphatic channel draining from the injection site to more than one sentinel node basins. Figure 1 shows the external iliac sentinel node showing fluorescence and the lymphatic track from the injection site leading onto the node. Details are presented in Table 2. Only 9 patients underwent bilateral pelvic node dissection due to failed sentinel node mapping.

Table 3 and Fig. 2 show the sites of sentinel node identified. For the 270 patients who had successful sentinel node mapping, there were 521 sites of sentinel nodes. Two hundred and sixty-one sites were identified on the right side and 263 on the left side. Obturator was the most common location (52%) followed by external iliac (34%). Para-aortic

Table 1 Clinicopathologic features of patients who underwent sentinel node mapping with ICG dye

Clinicopathological characteristics, n = 279	
Age in years (median with range)	61 (25–86)
BMI (median with range)	28 (19–59)
Pathologic diagnosis n (%)	
Carcinoma endometrium type 1 Grade 1 and 2	105 (37.6)
Carcinoma endometrium type 1 Grade 3	13 (4.9)
Carcinoma endometrium type 2	47 (16.8)
Carcinoma cervix	23 (8.3)
Endometrial hyperplasia	47 (16.8)

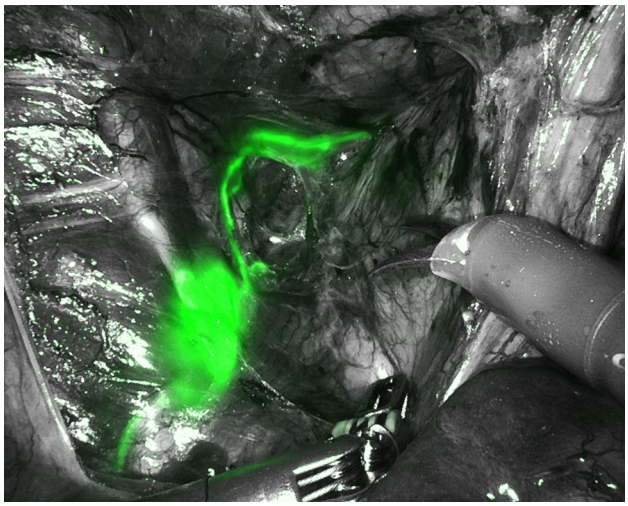

Fig. 1 Left pelvic side wall showing fluorescent lymphatic draining from the site of injection to the left external iliac node

Table 2 SLN mapping details

Details of sentinel lymphnode mapping n (%)	
Total number of patients with injected dye	279 (100)
Total number of patients with sentinel detected	270/279 (96.8)
Total number of patients with unilateral SLN mapping	40/270 (14.8)
Total number of patients with bilateral sentinel mapping	230/270 (85.2)
Total number of patients with separate tracts on hemipelvis	24/270 (8.9)

Table 3 Sentinel node location

Sentinel lymph node site	$N=521$
Obturator	271 (52%)
External iliac	177 (34%)
Internal iliac	33 (6.34%)
Parametrium	5 (0.95%)
Common iliac	15 (2.87%)
Para-aortic	14 (2.68%)
Presacral	6 (1.16%)

sentinel node was seen in 2.6% of patients and rare locations like pre-sacral and parametrial node were also noted during mapping. Twenty-eight (14%) patients with ca endometrium had a positive node on histopathology. None of the carcinoma cervix patients had positive nodes on pathologic examination.

Table 4 shows the sentinel node detection rates across different groups of patients. There was no significant difference in detection among patients with BMI less than 30 or more than 30. Same was scenario across different histological subtypes of carcinoma endometrium. Grade 3 Endometrioid carcinomas seemed to have a lower detection rate, but the difference did not reach statistical significance.

Discussion

Sentinel node mapping is emerging as a less invasive method of detecting lymph nodal metastases in endometrial and cervical cancers. Sentinel node mapping works on the concept that the sentinel node is the first node to which the organ drains and lymphatic dissemination of tumor happens in an orderly fashion affecting the first node and then subsequent nodes. So, if the first node, i.e., the sentinel node is negative for tumor metastases, the rest of the nodes will also be negative. Accurate identification of the sentinel node is very important as management markedly differs in node positive patients. Accurate surgical staging helps in delivering the correct adjuvant treatment for the patients [5].

Among the different tracers available for sentinel node mapping, ICG dye was found to have superior nodal detection rates [10]. Present study shows a detection rate of 96.8% as compared to the 86% detection rate reported in the FIRES trial [5]. Meta-analysis by Smith et al. shows average bilateral detection rate to be 75% when ICG was used. Present study shows a bilateral detection rate of 85.2% [11]. Higher detection rates meant that fewer number of patients needed lymphadenectomy during staging surgery thus minimizing the complications associated with lymphadenectomy in the majority of patients.

Sentinel node mapping was done in patients with atypical hyperplasia also as some patients with a preoperative diagnosis of atypical hyperplasia may have a postoperative diagnosis of endometrial carcinoma [12]. In the present study 4 patients (8.7%) with preoperative diagnosis of atypical hyperplasia had a diagnosis of malignancy in the hysterectomy specimen.

External iliac nodal basin was reported as the commonest site of sentinel node in many studies [4, 13] but present study found obturator as the most common location for sentinel node. Fifty-two percentage of patients in the current study has sentinel node located at the obturator nodal basin. ICG dye passes from the sentinel nodes to the nonsentinel nodes very fast and in this study, lymphatics were carefully traced to identify the sentinel node.

Histology and increased BMI were not found to be significantly associated with SLN detection in present study as well as in published literature [11]. Lowest detection rates (85.7%) were seen in Endometrioid Grade 3 histologies, but the results were not statistically significant. It was heartening to note that in obese patients also SLN mapping with ICG could detect sentinel node in 95% of the patients, limiting

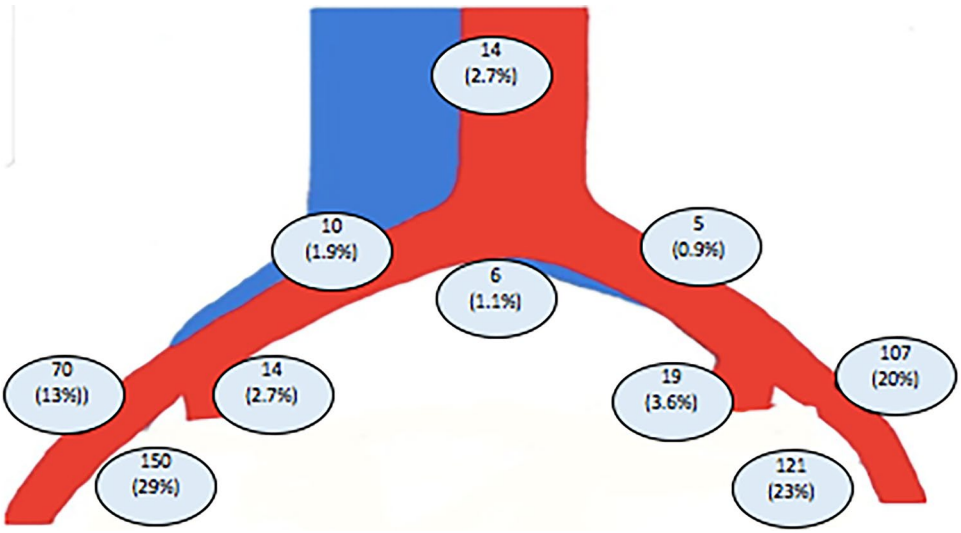

Fig. 2 Distribution of sentinel node detection sites in the pelvis

Table 4 Comparison of Sentinel node detection rates

	Sentinel detection rate *n* (%)	B/L SLN detection rate, *n* (%)	U/L SLN Detection rate, *n* (%)	*P* value
BMI (n = 279)				
Less than 30 (*n* = 198)	193 (97.4)	165 (83.3)	28 (14.1)	0.975
More than 30 (*n* = 81)	77 (95)	65 (80.2)	12 (14.8)	
Histology (n = 279)				
Ca endometrium Grade1 + grade2 (*n* = 148)	142 (95.9)	117 (79)	25 (16.8)	0.612
Grade3 (*n* = 14)	12 (85.7)	11 (78.5)	1 (7.2)	
Carcinoma endometrium type 2 (*n* = 47)	46 (97.8)	37 (78.7)	9 (19.1)	
Carcinoma Cervix (*n* = 23)	23 (100)	20 (87)	3 (13)	
Endometrial intraepithelial neoplasia (*n* = 47)	47 (100)	45 (96)	2 (4)	

the need for nodal dissection in only 5%. This is of great value as nodal dissection can be technically challenging in patients with higher BMI.

Conclusion

Sentinel node mapping using ICG dye has got excellent overall and bilateral detection rates making it a valuable tool in the surgical staging of endometrial and cervical cancers. Obturator was found to be the most common location for the sentinel node and it is important to trace the lymphatics to identify the sentinel node correctly while using ICG dye as multiple nodes can take up the tracer. Mapping using ICG dye yields good detection rates in all histologies of endometrial cancer and in patients with high BMI.

Author Contributions AR was involved in concept and design, manuscript preparation, manuscript review and also guarantor. AA and VP were involved in data acquisition and analysis. AR and AA were involved in manuscript editing.

Declaration

Conflict of interest Anupama Rajanbabu is a proctor and advanced trainer for robotic surgery. Rest of the authors have no conflicts of interest.

Ethical Standards This study used de-identified patient database. Therefore, this study did not require IRB review in accordance with Code of Federal Regulations,45 CFR 46.

Human and Animal Rights Human participants (Study started after Institutional ethics committee approval).

Consent to Participate Informed consent was obtained from all individual participants included in the study.

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About the Author

Dr. Anupama Rajanbabu is the Professor and HOD of Gynecologic Oncology at Amrita Institute of Medical Sciences, Kochi. She has done over 800 gynecologic robotic surgeries and has trained surgeons across India in robotic surgery. She is also a keen researcher with over 50 peer reviewed publications and 15 book chapters to her credit. She has done over 200 paper presentations in national and international conferences and has won several best paper awards.