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Full length article

A prospective evaluation of the sentinel node mapping algorithm in endometrial cancer and correlation of its performance against endometrial cancer risk subtypes

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ABSTRACT

Objective: Sentinel node mapping is emerging as the alternative to lymphadenectomy in endometrial cancer. The objective of our study is to validate of the sentinel node mapping surgical algorithm and also to compare the performance of the algorithm against endometrial cancer risk subtypes

Design: This is a prospective interventional study carried out at a Single University teaching hospital. All patients with apparent early stage endometrial cancer who underwent robotic assisted surgical staging were included. Intracervical injection of Indocyanine Green dye and sentinel node identification and biopsy was done for all study patients. The node positive rate when using SLN mapping alone versus SLN mapping algorithm were compared. The node positivity was compared against various risk subtypes of endometrial cancer.

Results: 69 patients were included in the study. In 95.7% patients SLN was detected with a bilateral detection rate of 87.9%. 10 patients had nodal positivity, among which 7 were identified by SLN mapping alone. The algorithm captured all 10 patients with positive LNs, yielding a node positivity rate of 14.9%, sensitivity and NPV of 100%. For SLN mapping alone the sensitivity was 77.8%, false negative rate (FNR) 22.2%, and NPV 96.6%. In low- and intermediate-risk subtypes SLN mapping as well as algorithm identified all node positive patients, but in high-risk endometrial cancers the SLN mapping technique alone had a sensitivity of 57.1% and false-negative rate of 42.9% when compared with 100% sensitivity for the SLN mapping algorithm.

Conclusions: When doing SLN mapping and biopsy during endometrial cancer staging surgery it is essential that the steps mentioned in the SLN mapping algorithm are followed as SLN mapping alone seems to have a limitation in detecting positive nodes especially in high risk subtypes of endometrial cancer. Even with the lack of survival data, based on the performance of SLN mapping surgical algorithm (even if ultrastaging facility is not available), it seems to be a better technique in detecting metastatic nodes, giving prognostic information, and enabling accurate adjuvant treatment.

Introduction

Lymphadenectomy is one of the most debated topics in endometrial cancer (EC) surgery with practices varying from avoiding lymphadenectomy in certain low risk groups, to complete pelvic and para aortic lymphadenectomy [1]. Lymph nodal involvement is one of the most important prognostic markers which guide adjuvant treatment and not having this information can lead to over or under treatment [2]. Sentinel Lymph node (SLN) mapping offers a middle ground here by providing the information on nodal status thus enabling correct adjuvant treatment but avoids the surgical morbidity of nodal dissection [1,3].

Several studies have investigated the role SLN mapping in EC using different methods (blue/technetium/indocyanine green fluorescence [ICG] detection with near infrared imaging [NIR]) [4–10]. The largest series on the validation of the SLN mapping surgical (SLNMS) algorithm using blue dye was from MSKCC [6]. B. Hagen et al. investigated the validity of MSKCC algorithm using the NIR/fluorescence robotic platform [9]. The multicentre prospective FIRES trial demonstrated the role of SLN biopsy in accurately staging endometrial cancer [10].

In this study we aimed to investigate the validity of SLNMS algorithm using ICG and NIR fluorescence imaging using robotic platform. We also investigated the performance of SLN mapping alone and SLNMS algorithm in various risk groups of endometrial cancer.

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Methods

This is a prospective interventional study conducted at Amrita Institute of Medical Sciences, Kerala, India, from March 2015 through September 2017 including patients with apparent early stage endometrial cancer undergoing robotic assisted staging surgery. This study was conducted after having validated the technique of SLN mapping using ICG and NIR imaging [11,12]. Ethical clearance was obtained from the institutional ethics committee.

Robotic-assisted laparoscopic surgery was performed with daVinci Xi Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), with SLNM performed after indocyanine green (ICG) injection followed by fluorescence detection using Near Infrared Imaging (NIR). Surgical staging included total hysterectomy, bilateral salpingo-oophorectomy, and mapping and removal of SLNs. Where SLN's were not detected, bilateral pelvic and paraaortic LND was done based on pre-operative risk factors (endometrial biopsy result and MRI staging).

All patients with histologically confirmed endometrial cancer who underwent robotic assisted surgical staging were included in the study. Patients with uterine sarcomas and with complex atypical hyperplasia were excluded.

Technique

25 mg vial of ICG powder (Aurolab, Madurai, India) was dissolved in sterile water to make 0.5% solution. Cervix was injected with 4 ml of ICG, 1 ml each at 3 and 9 o' clock position superficially and deep into cervical stroma. The abdomen and pelvis was assessed in NIR mode before and after opening the peritoneum in order to identify lymphatic channels leading to SLNs. The lymph node stations were dissected carefully to identify the sentinel nodes. Suspicious nodes found intraoperatively, were removed in addition to ICG fluorescence positive green SLNs. When SLN mapping in the pelvis was not obtained on one side, side specific pelvic lymph node dissection (LND) was performed. The number and location of excised SLNs and non SLNs were recorded. Histopathological details (histological type, grade, myometrial invasion, stage, tumour size, lymphovascular space invasion) were obtained from the pathology report.

Pathologic procedure

After formalin fixation, the nodes were embedded in paraffin blocks. Embedding done either *in toto*, or sectioned when lymph nodes are too large to fit into one block. SLNs and non SLNs were stained with H&E. All surgical specimen including lymph nodes, were examined by specialist gynecologic onco-pathologist. All lymph node metastases were measured in millimetres, and result were included in pathology. Ultra staging protocol for the examination of lymph nodes was not followed.

Various definitions used in the study are presented in Box 1. Each patient, rather than each hemi-pelvis was used as the site of analysis. Cases with bilateral failed mapping with no SLNs removed were considered non evaluable for analysis of SLN alone; cases with no LNs dissected (SLN or non-SLN) were considered non evaluable for analysis of the algorithm.

The risk stratification of EC patients into low, intermediate and high-risk was done following the PORTEC II risk stratification [13] on final histopathology specimen, based on which adjuvant treatment was decided.

Result

During the study period 69 patients with endometrial cancer underwent robotic assisted surgical staging with SLNM. Demographic and clinicopathologic characteristics of the study population are summarized in Table 1. The median age was 60 years (range, 30–82), with a median body mass index of 27.9 (range, 18.2–44.1). Histology was distributed as follows: endometroid, 58 (83.8%); serous, 7 (10.1%); clear cell, 2 (2.9%); carcinosarcoma, 2 (2.9%). Majority of the patients had stage I EC (51 [73.9%]).

Median SLN count was 5 (range, 1–14), and median total LN count was 11 (range 8–32). At least one SLN was detected in 66/69 patients (95.7%). There was unilateral mapping in 8/66 cases (12.1%), with 4/66 (6.06%) on the right, and 4/66 (6.06%) on the left. Bilateral pelvic mapping SLN detection rate was 58/66 (87.9%). Of the 66 patients with at least one SLN identified, 62 (94%) mapped only to pelvis, 2 (3%) mapped both to pelvis and to paraaortic region, and 2 (3%) has SLNs limited to paraaortic region only (Table 2).

Table 1
Demographic and clinicopathologic characteristics, N = 69.

Characteristic	Number of Patients (%)
Age, years Median (Range)	60 (30–82)
Body mass index, kg/m^2 Median (Range)	27.9 (18.2–44.1)
Histologic type	
Endometroid	58 (83.8%)
Serous	7 (10.1%)
Clear cell	2 (2.9%)
Carcinosarcoma	2 (2.9%)
FIGO Stage	
IA	33 (47.8%)
IB	18 (26.1%)
II	4 (5.8%)
IIIA	3 (4.3%)
IIIC	8 (11.6%)
IV	3 (4.4%)

Box 1. Definitions used in study.

SLN detection rate: Proportion of cases in which at least one SLN was identified among patients with attempted mapping.
Failed mapping: No SLN was detected.
True Negative: Negative SLN or algorithm in a patient with no nodal metastases.
False Negative: Histopathology negative SLN or node detected by algorithm in a patient with nodal metastases.
True Positive: Histopathology positive SLN or node detected following the algorithm in a patient with nodal metastases.
Sensitivity: Number of true positives divided by all patients with LN metastases.
False-negative rate (FNR): Number of false-negatives divided by the number of patients with LN metastases.
Negative predictive value (NPV): Number of true negatives divided by number of patients with a negative test (SLN alone or algorithm).
Node positivity rate (NPR): Proportion of cases with lymph node metastases among patients with at least one LN removed.
‡ False positive was impossible by definition.