



The importance of para-aortic lymph nodes in sentinel lymph node mapping for endometrial cancer by using hysteroscopic radio-isotope tracer injection combined with subserosal dye injection: Prospective study



Fumio Kataoka^{a,*}, Nobuyuki Susumu^a, Wataru Yamagami^a, Michiko Kuwahata^a, Aya Takigawa^a, Hiroyuki Nomura^a, Hiroya Takeuchi^b, Tadaki Nakahara^c, Kaori Kameyama^d, Daisuke Aoki^a

^a Department of Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan

^b Department of Surgery, Keio University School of Medicine, Tokyo, Japan

^c Department of Radiology, Keio University School of Medicine, Tokyo, Japan

^d Department of Diagnostic pathology, Keio University School of Medicine, Tokyo, Japan

HIGHLIGHTS

- We investigated diagnostic accuracy of SN mapping in endometrial cancer patients.
- Our SN mapping procedure showed a high detection rate, sensitivity, and NPV.
- We highlighted the importance of SN exploration in the para-aortic lymph nodes.

ARTICLE INFO

Article history:

Received 4 September 2015

Received in revised form 21 December 2015

Accepted 23 December 2015

Available online 28 December 2015

Keywords:

Endometrial cancer

Sentinel lymph node

Hysteroscopic

Para-aortic lymph node

ABSTRACT

Objective. The objective of this study is to evaluate the detection rate and diagnostic accuracy of sentinel lymph node (SN) mapping using hysteroscopic sub-endometrial injection of 99m-Tc-hexamethylphosphoramide (Radio-isotope; RI method) and subserosal Indocyanine green (ICG) injection (Dye method) in patients with endometrial cancer.

Methods. From April 2009 to December 2012, prospective evaluation of 57 Japanese endometrial cancer patients undergoing SN mapping using RI method combined with Dye method was done. To combine RI method or no was determined by a status of RI supply of the tracer injection day. As for 32 cases, both (RI + Dye) methods were used and 23 cases were performed only in Dye method. The primary endpoint was estimation of sensitivity and negative predictive value (NPV) of SN, and analysis of the distribution of SNs with metastasis.

Results. At least one SN was detected in 100% and average number of detected SNs was 6.0 in RI + Dye method. Sensitivity and NPV were 100%, 100%, respectively. From results of SN mapping, 62.8% of SNs were present in pelvic and 37.1% in para-aortic lymph nodes (PAN). Total 56.3% of lymph nodes with metastasis were present in pelvic and 43.8% in PAN, and the distribution has no difference with SN mapping results ($P = 0.602$). Among 13 cases with metastatic SNs, 76.9% cases showed metastasis in PAN.

Conclusions. This SN mapping procedure for endometrial cancer patients revealed high detection rate, sensitivity, NPV, and also indicated the importance of the SN exploration in PAN area.

© 2015 Elsevier Inc. All rights reserved.

1. Introduction

Endometrial cancer is the most common gynecologic cancer in developed countries [1]. Nodal status has been reported as an important prognostic factor of endometrial cancer, recently enhanced by the

introduction of the new FIGO classification which considers different stages according to the histological positivity in pelvic and para-aortic lymph nodes (PAN) [2]. However, two large randomized-control trials demonstrated that routine systematic lymphadenectomy did not improve the prognosis of endometrial cancer [2,3]. The appropriate extent of surgical staging for patients with endometrial cancer is controversial, ranging from complete pelvic and paraaortic lymphadenectomy to complete omission of lymphadenectomy [1]. Sentinel lymph node (SN) mapping has been well established in melanoma and breast cancer

* Corresponding author at: Department of Obstetrics and Gynecology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.
E-mail address: f-kata@a6.keio.jp (F. Kataoka).

[4,5] and also appears promising in vulvar cancer [6] and cervical cancer [7]. SN sampling may reduce the risk of complications such as blood vessel and nerve damage, lymphedema, and lymphocyst formation for patients with endometrial cancer by minimizing the disruption of lymphatic flow. In this study, we aimed to assess the diagnostic accuracy (detection rate, sensitivity and negative predictive value) of SN detection using hysteroscopic sub-endometrial injection of ^{99m}Tc -phytate combined with subserosal injection of Indocyanine green (ICG), and also aimed to clarify the significance of PAN exploration in SN mapping for endometrial cancer.

2. Materials and methods

2.1. Patients

After Institutional Review Board approval from Keio University School of Medicine, 57 Japanese patients were prospectively enrolled from April 2009 to December 2012, and all patients gave written informed consent. This study inclusion criteria were: patients with endometrial cancer verified by pathological diagnosis who are going to receive hysterectomy with retroperitoneal lymphadenectomy, clinical stage IA–II (FIGO2009) and confined to uterus by MRI and CT imaging, over 20 years old at the time when signed informed consent. Exclusion criteria were: patients who are Grade 1 endometrioid adenocarcinoma without muscular invasion at their preoperative evaluation with MRI, patients who are estimated to have obvious extrauterine spread at their preoperative evaluation with MRI and CT, patients who have suffered other malignancy within 5 years, perioperative findings of bulky lymph nodes or extrauterine dissemination, and double cancer. All cases were received open surgery, because laparoscopic surgery for endometrial cancer has not been approved as a medical service under health insurance in Japan until March 2014.

The patients underwent SN biopsy followed by abdominal modified radical hysterectomy or radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy with or without para-aortic lymphadenectomy. If any finding: metastasis to pelvic lymph node, metastasis to adnexal lesion, deep myometrial invasion >50%, pathological subtypes of poor-prognosis (ie. Grade 3, serous adenocarcinoma, clear cell adenocarcinoma) is confirmed during operation, para-aortic lymphadenectomy was performed.

2.2. SN mapping procedure

To combine RI method or no was determined randomly by a status of RI supply of the tracer injection day. As for 32 cases, both methods were used and 23 cases were performed only in Dye method. Due to insufficient manpower of radiologists, administration of radioisotope to gynecologic cancer patient was possible only once a week.

2.3. Dye method

During operation, indocyanine green (ICG) was injected subserosally at 5 points of uterine corpus, and dye uptake was detected by macroscopic observation (observation by the naked eye). Six minutes after injection, retroperitoneal spaces were then opened and retroperitoneal sentinel dye-containing nodes were detected macroscopically. When identified, these nodes were marked with ligation approximately within 30 min after the injection.

2.4. RI method and lymphoscintigraphic technique

Previous day of surgery (16 h before operation), ^{99m}Tc -labeled phytate was injected into the sub-endometrium at 5 points (0.2 mL \times 5, total 2 mCi) just around the tumor using hysteroscopy of a 6.5 mm operative hysteroscope (Olympus, Tokyo, Japan)

after cervical dilation under anesthesia. Preoperative lymphoscintigraphy was obtained 15 h after the tracer injection.

Intraoperative radio-labeled SN sampling was performed using a handheld gamma probe (GPS Navigator, Tyco Healthcare, Tokyo, Japan).

2.5. Pathological evaluation

Intra-operative frozen section diagnosis of the SNs was performed in every case. Pathologic ultrastaging was performed, with multiple serial sectioning of the entire sentinel lymph node at 200 to 300 μm , with 3 consecutive HE levels with one slide for immunostaining per level. Immunostaining for cytokeratin (clone AE1/AE3, Milipore Inc., dilution 1:150) was performed in SNs after HE routine histological examination. Non-SNs were processed using entire node examination with HE staining. Macrometastases were considered as tumor foci larger than 2 mm, whereas micrometastases were considered as tumor foci between 0.2 mm and 2 mm. Isolated tumor cells (ITC) were defined as deposits less than 0.2 mm.

2.6. Statistical analysis

Statistical analysis of the data was performed using the unpaired Student *t* test, the Chi-square test, Mann–Whitney *U* test. All statistical analyses were performed using the SAS 9.2 statistical package (SAS Institute, Cary, NC), and all P-values that were 2-sided at a value of <0.05 were considered to be statistically significant.

3. Results

Initially 57 patients were enrolled to this study. According to the eligibility criteria 2 patients were excluded. One patient had peritoneal dissemination, and one patient was diagnosed as double cancer of endometrial cancer and ovarian cancer. In total 55 cases were included into the study. RI + Dye method were used in 32 cases and 23 cases

Table 1
Characteristics of eligible 55 patients.

Characteristics	RI + Dye (n = 32)	Dye only (n = 23)	P value
Age, years			0.53
Median (range)	54(30–77)	54(27–76)	
FIGO stage 2009			0.50
IA	15	14	
IB	2	3	
II	3	1	
IIIA	3	0	
IIIB	1	0	
IIIC1	1	2	
IIIC2	7	3	
Histology			0.38
Endometrioid	27	22	
Serous	2	0	
Mixed	3	1	
Grading			0.27
1	4	7	
2	20	13	
3	8	3	
Lymphovascular space invasion			0.42
Present	18	10	
Absent	14	13	
Type of hysterectomy			1.00
Modified radical hysterectomy	30	22	
Radical hysterectomy	2	1	
Lymphadenectomy			0.40
Pelvic	18	16	
Pelvic + Para-aortic	14	7	

RI + Dye; Hysteroscopic sub-endometrial injection of ^{99m}Tc -labeled phytate (RI method) and ICG injection (Dye method).

Download English Version:

<https://daneshyari.com/en/article/3942968>

Download Persian Version:

<https://daneshyari.com/article/3942968>

[Daneshyari.com](https://daneshyari.com)