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Original

Preoperative detection of sentinel lymph node in patients with endometrial cancer — comparison of planar lymphoscintigraphy, SPECT and SPECT/CT

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Abstract

Background: Sentinel lymph node (SLN) mapping allows minimal invasive assessment of lymph node status in patients with early-stage endometrial cancer (EC). Intraoperative detection of SLNs is based on the results obtained from preoperative nuclear medical images. The purpose of this study was to compare the data obtained from planar lymphoscintigraphy (PL), single-photon emission computed tomography (SPECT), and SPECT with computed tomography (SPECT/CT) for preoperative SLN detection in patients with EC.

Material and methods: A total of 44 images in 22 patients with early-stage EC (22 PL, 9 SPECT and 13 SPECT/CT) were analyzed. The scans were performed in the period 2018–2020 at the Institute of Pathophysiology and Nuclear Medicine in Skopje. Thirteen patients underwent PL and SPECT/CT and nine patients underwent PL and SPECT after cervical injection of 4 mCi ^{99m}Tc-SENTI-SCINT on the day of surgery. Descriptive statistics, Wilcoxon Matched Pairs Test, and Spearman rank R coefficient were used for data analyses.

Results: Twenty-two patients with mean age of 61.1 ± 7.5 and body mass index (BMI) 34.62 ± 6.4 kg/m^2 were included in the study. In four patients (18.2%) SLN was not detected on PL. Detection rate on SPECT and SPECT/CT was 100%. The average number of detected SLN was 1.4 ± 1.05, 2.2 ± 1.1 и 2.15 ± 1.1 on PL, SPECT and SPECT/CT respectively. We found a statistically significant difference in the number of detected SLNs on PL *vs.* SPECT/CT ($p = 0.0077$). The most common SLN location on SPECT/CT was the right internal iliac followed by the left common iliac region.

Conclusions: The results of the presented study indicate a higher diagnostic value of SPECT/CT in terms of SLN detection and exact anatomic localization as compared to planar lymphoscintigraphy (PL).

KEY words: sentinel lymph node; lymphoscintigraphy; SPECT/CT; endometrial cancer

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Introduction

Detection of a sentinel gland or a sentinel lymph node (SLN) allows the removal of the first drainage lymph node from the region of the malignant lesion. If no malignant cells are detected in this node, it is assumed that the other lymph nodes of the same lymph path are not affected by metastatic deposits as well [1]. Detection and biopsy of a sentinel gland are part of the standard surgical protocol for assessing nodal status in patients with early-stage breast cancer and malignant melanoma [2, 3]. In recent years, the number of published data in the literature for detection of a SLN in patients with endometrial cancer (EC) has increased. The interest in introducing the SLN concept in these patients is due, above all, to the minimally invasive approach to assessing lymph node status by reducing the morbidity associated with radical lymph node dissection [4–6].

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The nuclear medicine procedure for preoperative mapping of the lymphatic drainage in EC is performed by using colloidal tracers labeled with Technetium-99m (^{99m}Tc), applied with cervical, subendometrial/peritumoral, or subserosal/myometrial injection [7]. The cervical method of tracer application is most commonly used because of the simple approach and the highest pelvic detection rate [8]. The tracer is usually administered on the day of the intervention.

Intraoperative detection of the SLN is based on the results obtained from its preoperative localization on nuclear medicine images. Conventional planar lymphoscintigraphy (PL), through dynamic and static imaging in multiple positions, provides a two-dimensional display of lymphatic drainage and the SLN. Single-photon emission computed tomography (SPECT) through the acquisition of multiple cross-sections, allows obtaining a three-dimensional image which increases the sensitivity, and in combination with computed tomography as hybrid SPECT/CT technology provides more accurate anatomical localization of the SLN [9–11]. Identification of the SLN leads to its simpler and faster detection, and also to a reduction in the extent of surgery. The aim of this study was to analyze and compare the data of the SLN in patients with early-stage EC, obtained with different techniques of nuclear medicine imaging: PL, SPECT and SPECT/CT.

Material and methods

A prospective, randomized study was conducted at the Institute of Pathophysiology and Nuclear Medicine, Faculty of Medicine “Ss. Cyril and Methodius” in Skopje, in the period March 2018–December 2020. The study analyzed a total of 44 nuclear medical images (22 PL, 9 SPECT, and 13 SPECT/CT) in 22 patients with EC in the preoperative first stage of the disease. The patients were recruited at the University Clinic for Gynecology and Obstetrics in Skopje. The study included patients with histologically verified EC (endometrioid adenocarcinoma of grade 1 and 2) at a presumed first stage of the disease (based on preoperative evaluation) T1; N0; M0. All patients have signed informed consent for the procedures and participation in the study, which was approved by the Ethics Committee of the Medical Faculty in Skopje.

Procedure

^{99m}Tc-SENTI SCINT (commercial kit of MEDI-RADIOPHARMA LTD, Hungary) was applied to all patients in the morning on the day of surgery with cervical injection in four quadrants at a depth of 5 mm: 1 mCi (37 Mbq) × 4 injections (total dose per patient 4 mCi). The application of ^{99m}Tc-SENTI SCINT was performed by a specialist in gynecology and obstetrics. After the application of the tracer, PL and SPECT were performed in 9 patients, while PL and SPECT/CT were performed in 13 patients, according to the following acquisition protocol:

- dynamic study after the application of the radiopharmaceutical (30 frames, 60 seconds per frame);
- static images for 30 minutes, 60 minutes, and 120 minutes (600 seconds/image);
- SPECT or SPECT/CT after 120–180 minutes:
  - SPECT (60 projections for 15 seconds per projection, angle per projection: 6 degrees, angle per detector: 180 degrees, matrix 128 × 128);
  - CT (matrix 512 × 512, rotation time: 1 second, cross-sectional thickness: 2.5 mm, cross-sectional distance 2.5 mm).

During the performance of the nuclear medicine methods, the principle ALARA (as low as reasonably achievable) was fully observed, i.e. the smallest dose of radiopharmaceutical was used to visualize the SLN on PL, SPECT and SPECT/CT. All static images were taken using a Mediso DHV Nucline Spirit dual-head gamma camera. SPECT and SPECT/CT were performed using the SPECT/CT camera OPTIMA NM/CT 640 GE Healthcare dual detector/4 slice CT.

After SLN identification in nuclear medicine imaging, all patients were operated at the University Clinic for Gynecology and Obstetrics in Skopje, in accordance with the operating protocols of the Clinic.

Nuclear medicine images were analyzed in terms of display of the SLN, number of SLNs, time of visualization of the SLN after application of the tracer, localization of the SLN (unilateral pelvic, bilateral pelvic, para-aortic), and pelvic localization of the SLN by anatomical regions, which is possible only on SPECT/CT.

Statistical data analysis

A database was created for statistical data processing in the statistical program SPSS for Windows 23.0. Category variables are presented by absolute and relative numbers, quantitative variables are presented by descriptive parameters (mean, SD, minimum, maximum). The detection rate of the SLN in nuclear medicine images is shown as the total detection rate (defined as the ratio between the number of patients with at least 1 detected SLN in a nuclear medicine image and the total number of subjects in the study), bilateral detection rate (defined as the ratio between the number of patients with at least 1 SLN detected in the two hemipelvic regions and the total number of participants in the study), the detection rate of PL, SPECT, SPECT/CT; total detection rate of para-aortic SLN (defined as the ratio between the number of patients with at least 1 detected SLN in the para-aortic region in nuclear medicine imaging and the total number of participants in the study).

To compare the number of SLNs among the techniques performed, a non-parametric Wilcoxon Matched pairs test was used. A non-parametric correlation test (Spearman rank R coefficient) was used to correlate age and BMI with the number of SLNs on PL and the time of onset of the SLN after application of ^{99m}Tc-SENTI-SCINT. For the level of significance, the value of $p < 0.05$ is taken.

Results

The study included a total of 22 female patients with histologically verified endometrioid adenocarcinoma (grade 1) — 7 patients, and (grade 2) — 15 patients, aged 46 to 74 years, with an average age of 61.1 ± 7.5 years. The body mass index (BMI) had an average value of 34.62 ± 6.4 kg/m^2, and ranged from 23.4 to 53.3 kg/m^2.

In 4 patients (18.2%), the SLN was not detected on the planar image. In all patients with SPECT or SPECT/CT pelvic SLNs were detected (Fig. 1). The total detection rate was 100%, bilateral detection rate was 31.81%, detection rate of PL was 81.81%, while for SPECT and SPECT/CT it was 100%. The total detection rate of para-aortic SLNs was 22.72%. On the PL, the most common finding was one SLN in 9 patients (40.9%), while on SPECT/CT the finding of two SLNs was most common, in 5 patients (38.5%). The total number

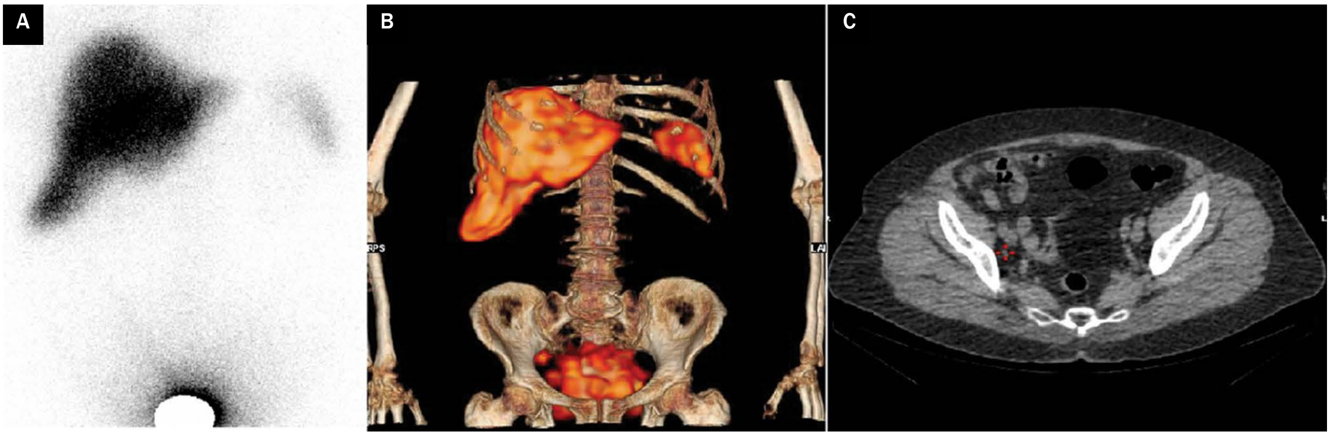

Figure 1. Planar lymphoscintigraphy (PL) and SPECT/CT in a 67-year-old patient with grade 2 endometrial adenocarcinoma; PL (**A**) did not show activity corresponding to a SLN. The fused SPECT/CT image (**B**) showed a focal accumulation in the right hemipelvic region, corresponding to two, non-enlarged lymph nodes in the right internal iliac region at the CT (**C**)

Table 1. Distribution of patients by number of detected SLNs on nuclear medicine imaging

Visualization of the SLN on a gamma camera	Number of SLNs		
	PL n (%)	SPECT n (%)	SPECT/CT n (%)
No SLN is shown	4 (18.18)		
One SLN is shown	9 (40.91)	3 (33.33)	4 (30.77)
Two SLNs are shown	6 (27.27)	2 (22.22)	5 (38.47)
Three SLNs are shown	2 (9.09)	3 (33.33)	2 (15.38)
Four SLNs are shown	1 (4.54)	1 (11.11)	2 (15.38)
Total number of shown SLNs	31	20	28

PL — planar lymphoscintigraphy; SLN — sentinel lymph node; SPECT/CT — single photon emission computed tomography/computed tomography

Table 2. Distribution of the SLNs in the pelvis by anatomical regions

Anatomical location of the SLN in the pelvis	Number of SLNs
Right obturator region	2
Left obturator region	1
Right external iliac region	2
Left external iliac region	2
Right internal iliac region	7
Left internal iliac region	1
Right common iliac region	2
Left common iliac region	6
Right para-aortic region	3

SLN — sentinel lymph node

of detected SLNs was 31 on PL, 20 on SPECT, and 28 on SPECT/CT (Tab. 1). The average number of detected SLNs was 1.4 ± 1.05, 2.2 ± 1.1, and 2.15. 1.1, respectively, on PL, SPECT, and SPECT/CT.

According to the results of the statistical analysis, the difference in the number of SLNs detected on PL and SPECT was not statistically significant (15 SLNs detected on PL *vs.* 20 SLNs detected on SPECT in 9 patients; $p = 0.068$), while the difference in the number of SLNs detected on PL and SPECT/CT was confirmed as statistically significant, for $p = 0.0077$ (16 SLNs detected on PL *vs.* 28 SLNs detected on SPECT/CT in 13 patients).The analyzed correlations between age and BMI, with the number of SLNs visualized on PL and with the time of presentation of SLNs after application of ^{99m}Tc-SENTI-SCINT, were statistically insignificant.

The most common anatomical location of the SLNs in the pelvis in the group of patients with SPECT/CT was the right internal iliac region followed by the left common iliac region (Fig. 1). Data on the anatomical location of the SLNs is shown in Table 2.

Discussion

Endometrial cancer (EC) is the sixth most commonly diagnosed cancer in women and the second most common cancer of the female genital tract in developing and underdeveloped countries. According to Global cancer statistics 2020: GLOBOCAN, there is a growing trend of EC worldwide with increasing morbidity and mortality (417,367 new cases of EC were registered in 2020, of which 97,370 ended in death) [12]. About 80 percent of diagnosed cases are in the early stages of the disease. Obesity and advanced age are significant risk factors associated with the endometrioid type of EC [13]. Our study included patients in the preoperative first stage of the disease, with histologically verified endometrioid type of adenocarcinoma, with a grade 1 and 2. A total of seven patients had EC with grade 1 and fifteen patients had EC with grade 2. The average age of patients was 61.1 ± 7.5 years, and 90% of them were over 50 years of age. These data are correlated with the already published epidemiological data in the literature [13]. Patients diagnosed at an early stage of the disease have a good prognosis, with a 5-year survival of about 90%, compared with patients with nodal metastases having a 5-year survival of about 60% [14, 15]. Nodal status is the most important prognostic factor for relapse and an indicator on which further oncological therapy is based. SLN biopsy is a minimally invasive method for determining the nodal status of patients with early-stage EC [16].

The detection rate of the SLN with cervical tracer application ranges from 67% to 85.7% for PL, and 84% to 100% for SPECT/CT (10, 17–20). The total rate of preoperative detection of the SLN in our study was 100%, the rate of bilateral detection was 31.81%, while the individual detection rate of PL, SPECT and SPECT/CT was 81.81%, 100%, and 100% respectively. The total detection rate of para-aortic SLNs was 22.72%. The number of SLNs detected on SPECT/CT was statistically higher than the PL, which corresponds to the literature data in addition to the significantly higher detection rate of SPECT/CT [20, 21].

In 2012, Kraft and Havel [22] published a study on the impact of age and obesity on the detection rate of PL and SPECT/CT in 69 patients with gynecological tumors. The authors found that younger age was associated with a higher rate of detection of SLNs as opposed to obesity, which had no effect on the study population. The analyzed correlation between age and BMI with the number of SLNs on PL in our study was statistically insignificant.

Lymphatic drainage mapping using the nuclear medicine method for SLN visualization in the correct anatomical region enables faster and more accurate localization of the SLN with the help of the gamma detection probe. The increased sensitivity with the application of SPECT is complemented by the precise localization and morphofunctional assessment provided by SPECT/CT. In most patients, the SLN is found in the external iliac region and the obturator region [19, 23]. In our study, the precise anatomical location of the SLN was confirmed intraoperatively in all thirteen patients with SPECT/CT. The most common location was the right internal iliac followed by the left common iliac region.

Conclusions

The results of our study indicate an advantage of the SPECT/CT modality over the detection rate of planar lymphoscintigraphy or SPECT alone, greater sensitivity in detecting SLNs with low activity and precise anatomical localization. We recommend SPECT/CT as the modality of choice in the preoperative SLN mapping in patients with EC.

Conflict of interest

The authors have no conflicts of interest to declare.

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