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Follow the River to the Lake: Sentinel Lymph Node Identification Using the Robotic Platform in Endometrial Cancer Patients

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Rezumat

Identificarea ganglionului santinelă în managementul cancerului endometrial

Biopsia ganglionului santinelă a fost introdusă în stadializarea chirurgicală a pacienților diagnosticați cu cancer endometrial. Numeroase studii şi ghiduri au stabilit că biopsia ganglionului santinelă este o procedură eficientă şi sigură din punct de vedere oncologic. Scopul acestui articol este de a sumariza cele mai importante recomandări pentru optimizarea identificării şi disecției ganglionului santinelă, pe baza experienței proprii. Fiecare etapă a tehnicii de identificare a ganglionului santinelă este analizată. Sfaturi şi trucuri, cum ar fi locul şi momentul injectării colorantului verde de indocianină sunt esențiale în identificarea optimă a ganglionului limfatic santinelă la pacienții cu cancer endometrial. Standardizarea tehnicii şi recunoaşterea reperelor anatomice sunt esențiale deoarece conduc la îmbunătățirea şi eficientizarea identificării ganglionului santinelă.

Cuvinte cheie: biopsia ganglionului santinelă, cancer endometrial, colorant verde de indocianin

Abstract

Sentinel lymph node biopsy for the management of endometrial cancer patients has been introduced into surgical staging of these patients. Several articles and guidelines have evaluated and found sentinel lymph node biopsy as an efficient and oncological safe

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procedure. The aim of this article is to highlight the most important tips and tricks in order to optimize sentinel lymph node identification and dissection based on our experience. Each step of sentinel lymph node identification technique is analyzed. Tips and tricks, such as site and time of indocyanine green dye injection are essential in optimal identification of sentinel lymph node in patients with endometrial cancer. The standardization of the technique and the recognition of anatomic landmarks are essential as they lead to an improved and effective identification of sentinel lymph node.

Key words: sentinel lymph node biopsy, endometrial cancer, indocyanine green dye

Introduction

Endometrial cancer remains the sixth most commonly diagnosed cancer in women worldwide, with an increased incidence rate in high/very high human development index countries compared to low/medium human development index countries. In 2020 it was estimated that more than 410,000 new cases were diagnosed worldwide and more than 97.000 deaths occurred due to this malignancy, with the incidence rate of Northern America and Europe to be on the top of worldwide regions incidence (1). The incidence of endometrial cancer is raising due to the increase in the number of overweight women, especially in patients with type I endometrial cancer which is estrogen dependent. Fortunately, the majority of patients usually seek medical attention early due to symptoms leading to early detection of this malignancy. Because of that, surgical treatment alone in the majority of patients, especially in patients with type I endometrial cancer, is curative. On the contrary, patients with type II endometrial cancer or advanced stage disease have poorer prognosis and depending on the stage they will need adjuvant therapy with chemotherapy and/or radiation (2).

Several prospective studies have confirmed the role of surgical treatment and staging in the management of endometrial cancer patients. Surgical treatment for these patients depends on the histopathological and imaging findings. Moreover, fertility sparing desire should be taken into account, especially in young endometrial cancer patients with early staged disease (3). Furthermore, the European Society of Gynecologic Oncology (ESGO) in collaboration with the European Society for Radiotherapy and Oncology (ESTRO) and the European Society of Pathology (ESP) have concluded in their latest guidelines for the management of patients with endometrial cancer that surgical treatment of apparent stage I/II endometrial carcinomas could be done by minimally invasive approaches, such as laparoscopic or robotic (2). Part of the surgical treatment for these early staged patients should include sentinel lymph node assessment and biopsy in order to evaluate the possible lymph node metastatic status and the necessity for adjuvant radiotherapy. The latest ESGO guidelines mentioned the utility of sentinel lymph node biopsy for staging purposes in patients with low and intermediate risk endometrial cancer. Several articles have investigated the feasibility and most efficient way of identification of the sentinel lymph node (4,5). The results of these studies led the authors of these guidelines to suggest that sentinel lymph node identification is preferably done by the use of indocyanine green with cervical injection (2).

Our department is the only state financed in Greece equipped with a daVinci X Surgical System and the Gynecologic Oncology Team have completed over 100 robotic assisted laparoscopic gynecological procedures for the

treatment of either benign or malignant pathologies since January of 2020. Moreover, in over 20 of them sentinel lymph node biopsy using indocyanine green fluorescence dye have been used.

Based on our experience, the aim of this article is to present our tips and tricks regarding the sentinel lymph node identification and biopsy using minimally invasive surgical approaches, especially using the robotic platform, in endometrial cancer patients.

Surgical Technique

Patients' Selection, Patients' Preparation

As referred, endometrial cancer patients' selection that would be appropriate for minimally invasive surgical treatment and sentinel lymph node biopsy for staging purposes are conducted based on histopathological and imaging examinations. Preoperative imaging staging is based on lower abdomen magnetic resonance imaging (MRI), upper abdomen computerized tomography (CT), and chest x-ray. Patients who suffered from other than endometrioid type endometrial cancer were not treated using sentinel lymph node biopsy and underwent systematic pelvic and para-aortic lymph node dissection (2). Moreover, our research team have created and recently published a preoperative score that evaluates the feasibility and predicts the duration of robotic gynecological surgeries (6). Based on the Iavazzo score, patients, who were graded with an Iavazzo score more than 8, were informed about the possibility of conversion to laparotomy if the robotic approach would be found to be unattainable.

All patients before the surgery signed an informed consent about the use of their characteristics and the possible visual documentation of their procedure. Our study was approved by Ethics and Research Board of our hospital.

The basic steps of patients' preparation as well as some tips and tricks about a successful robotic gynecological surgery were described by our research team in a previous published article (7). Briefly, these robotic procedures were conducted using all the 4 arms of Da Vinci Surgical System in a single line at the height of the umbilicus and a single laparoscopic port at the left lateral border of rectus abdominis muscle for assistance, using side docking for the patient cart. All the MIS procedures were conducted using uterine manipulator and/or McCartney tube in Trendelenburg position.

Based on the enhanced recovery protocol for minimally invasive gynecologic surgery, the patients could consume low fat solid food up to 6 hours prior to the induction to the anesthesia, while up to 2 hours before the surgery they should consume clear liquids enriched with carbohydrates. No mechanical bowel preparation was offered based on several guidelines. In order to prevent surgical site infections, patients are urged to use chlorhexidine 4% wash the night before and the morning of surgery. Moreover, skin and vaginal preparation intraoperatively with chlorhexidine 4% is done, without hair shaving (8).

Results

In total, 22 patients with endometrial cancer were treated robotically in our Department since January 2020 when the DaVinci robotic platform was established. Patients' characteristics are presented in *Table 1*. Nine patients were staged as endometrial cancer IA, while 13 patients as endometrial cancer stage IB. None of the patients in our cohort was upstaged surgically compared to preoperative staging. Furthermore, 3 patients who were preoperatively staged as endometrial cancer stage IB based on MRI imaging, were downstaged to IA through pathological examination of the surgical specimen.

Regarding the effectiveness of sentinel lymph node mapping and identification of sentinel lymph nodes, we did not manage to find any sentinel lymph node in 4 patients (18.2%) based on pathological findings. We

Table 1. Patients' characteristics

Patients' characteristics	No of patients (N:22)
Stage IA	9
Stage IB	13
Bilateral SLN identification	15
Unilateral SLN identification	3
Unsuccessful SLN identification	4

must mention that 3 out of these unsuccessful identifications were done in our first 10 cases of sentinel lymph node mapping. Bilateral sentinel lymph node identification was achieved in 15 patients (68.2%), while unilateral identification was recorded in 3 patients (13.6%).

In all the patients that successful lymph node mapping was achieved, the sentinel node was found in the upper paracervical pathway (9). More specifically, in 9 patients sentinel nodes were found in the external iliac artery area, in 5 patients in the internal iliac vessels area, while in 4 patients the sentinel node was found at the obturator fossa. Regarding the number of sentinel lymph nodes that were excised, at least 2 lymph nodes (mean value: 2.8 lymph nodes) were identified histopathologically in patients in whom bilateral identification was achieved. No complications related to the procedure were reported.

Lymph Node Mapping and Sentinel Lymph Node Identification

The patient is positioned in a modified lithotomy position with her legs on Allen stirrups. Injection is made based on recommendation from the Society of Gynecologic Oncology (10). More specifically, a vial containing 25 mg of indocyanine green dye fluorescence dissolved with 20 ml of sterile water is used in order to achieve a concentration of 1.25 mg/ml. Intracervical injection is preferred with a total of 4 ml to be used. The intracervical injection is made using a 25-gauge spinal needle. One ml of ICG solution is injected superficially and 1 ml deeper into the cervical stroma at the 3 and 9 o'clock position of ectocervix (*Fig. 1*).

Based on our experience, injection of ICG is better to be done right before the beginning of the surgery. That means right after the trocar placement in a laparoscopic procedure and right after the patient cart docking in a robotic surgical procedure. This approach seems to be more efficient regarding sentinel lymph node identification without the necessity of tracer re-injection. If the sentinel lymph node is not visualized after the first injection, additional 4 ml could be re-injected (2). Sentinel lymph node should be identified following the drainage pathways that spring from the bilateral parametria (*Fig. 2*). It is paramount that lymphatic vessels during the evaluation of parametria should be intact, integrity of lymphatic vessels should be preserved. Therefore, ligation of both round ligaments of the uterus should be done without any further tissue manipulation. The most proximal lymph node following the sentinel lymphatic vessel pathway should be dissected and be sent as sentinel lymph node for histopathological examination (*Table 2, Fig. 3*). Routine frozen section of sentinel lymph node is discouraged due to low sensitively. However, ultrastaging should be routinely part of

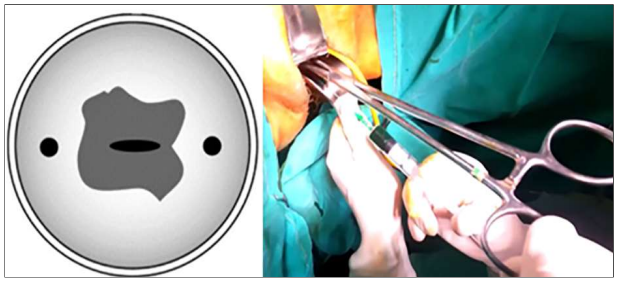


Figure 1. Schematic cervical injection sites and operative picture of injection.

Table 2. Step by step sentinel lymph node identification and biopsy by minimally invasive surgery for endometrial cancer

• Dilution of ICG: 1.25mg/ml
• Trocar placement, docking of patient cart
• Cervical injection at 3 and 9 o'clock – 1ml superficial and 1ml deeper into cervical stroma
• Atraumatic dissection of paravesical space
• Identification of anatomical structures (ureter, obliterated umbilical artery, external iliac vessels)
• Use of fluorescence imaging
• Identification of sentinel lymph node
• Dissection of sentinel lymph node and histopathological examination

ICG: indocyanine green fluorescence dye

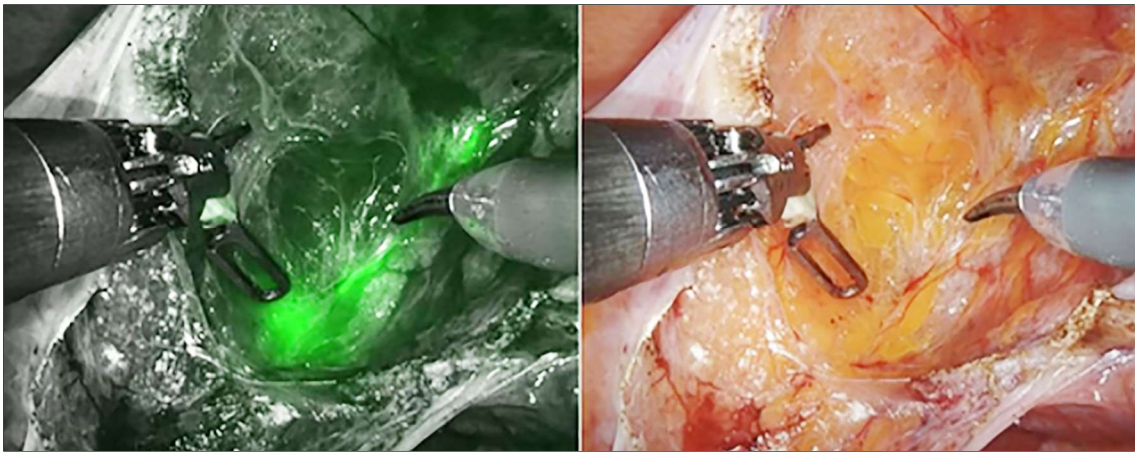


Figure 2. Robotic sentinel lymph node identification with and without fluorescence imaging ("Follow the river to the lake")

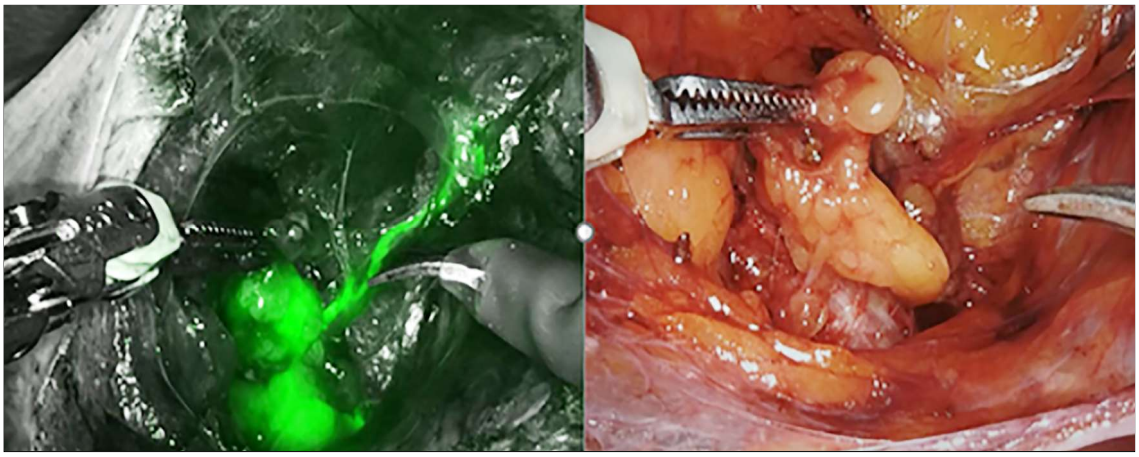


Figure 3. Robotic sentinel lymph node dissection with and without fluorescence imaging

histopathological examination of lymph node evaluation.

Discussion

The last decade several articles have investigated utility and oncological safety of sentinel lymph node biopsy, since its introduction in the management of gynecological oncology patients. The latest ESGO-ESTRO-ESP guidelines for the management of endometrial cancer patients conclude that sentinel lymph node biopsy could be considered for staging purposes in patients with low or intermediate risk disease, while indocyanine green dry fluorescence should be preferred due its higher sentinel lymph node identification rates (2).

Lymphatic drainage of the cervix follows a certain path through the parametrium to the iliac vessels area and the obturator fossa. Sentinel lymph node most common sites (80.6%) are the external iliac area and the internal iliac area. Other less common sites are the presacral, the common iliac and the para-aortic area (8-10%) (11).

Sentinel lymph node identification using ICG have been found to be the most effective regarding lymph node identification when compared to methylene blue or technetium approach (12,13). Regarding the detection rate and the sensitivity of sentinel lymph node mapping, a multicenter prospective

cohort study with clinical stage I endometrial cancer reported a 86% of successful mapping, while only 3% of patients with positive lymphatic disease were not diagnosed through sentinel lymph node biopsy (14). Moreover, Abu Rustum et al., who first described the procedure of sentinel lymph node mapping in endometrial cancer patients, reported a learning curve of 30 cases in order to achieve an increase in identification from 77 to 94% (15). Despite the fact that our cohort is relatively small, our data analysis showed an identification rate of 77.2%. Moreover, we have to mention that 3 out of 5 unsuccessful attempts to identify a sentinel lymph node occurred in our first 10 cases. In all of these attempts we were misled by the "empty package" effect, where we excised an ostensible sentinel lymph node that pathologically was found to be enlarged lymphatic vessels.

Based on our experience, we concluded to the aforementioned tips and tricks that would probably lead to a successful sentinel lymph node identification using the robotic daVinci X platform in patients with endometrial cancer. We found out that injecting the ICG before the trocar placement and docking the patient cart would minimize the possibility of identification of sentinel lymph node. Therefore, we suggest that injection should be made after the trocar placement and docking of the patient cart, especially during the learning curve period when the docking could be time consuming. Moreover, our retrospective analysis showed that using anatomical landmarks such as the ureter, the iliac vessels, and the obliterated umbilical artery could lead to an easier and faster sentinel lymph node identification without any excessive dissection.

Our study presents some strengths and some limitations that should be mentioned. Strengths of our study should be the correct patient selection using some preoperative tools such as Iavazzo's score and the presentation of real-life experiences of a single robotic center. The retrospective character of our study and the small sample of our cohort should be documented as limitations of our study.

Conclusion

By suggesting our tips and tricks to literature, we aim to minimize the failure rates of sentinel lymph node identification and to achieve a quicker learning curve.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Author's Contributions

Christos Iavazzo: concept visualization, supervision, manuscript revision. Alexandros Fotiou: manuscript writing, data selection. Kalliopi Kokkali: manuscript writing, data selection. George Vorgias: supervision, manuscript revision.

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