Identification of the Parametrial Nodes through Lymphatic Mapping: What is the First Sentinel Nodal Station in Women with Cervical Cancer?

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Abstract

Background: Sentinel lymph node (SLN) mapping, although considered still in an experimental phase, is becoming an increasingly popular procedure for the management of selected cervical cancer patients. Despite paracervical lymphatic tissue being the first pathway of tumour spread, in the vast majority of cases the first SLN is found among the interiliac nodes. With this surgical video we aimed to show the identification of the SLN through robotics and colorimetric lymphatic mapping with blue dye.

Methods: SLN mapping was performed with methylene blue dye colorimetric technique. SLN biopsy was performed through robotic approach with identification of SLN in the parametrial and interiliac regions. The SLN received an ultra staging processing.

Results: The video shows the identification of the SLN after blue dye mapping. Two pelvic SLN were identified on the right size and 3 on the left size. Identification and isolation of the parametrial node as well as of the lymphatic trunks is demonstrated.

Conclusions: The identification of Parametrial SLN after blue dye injection is technically feasible also through a robotic approach. Larger series are however needed to clarify their prognostic role. It is our hope that this video may push forward the discussion on this issue.

Keywords: *Robotic-assisted laparoscopic surgery; cervical cancer; sentinel lymph node (SLN); pelvic lymphadenectomy*

Introduction

Since Wertheim's first report, radical hysterectomy together with systematic pelvic lymphadenectomy has represented the gold standard procedure for the surgical management of cervical cancer [1-3]. Nevertheless, the surgical morbidity related to these combined procedures, especially in terms of urinary dysfunctions and lymphedema, which may in the long run impair women's quality of life, had progressively powered several studies to investigate the feasibility and safety of less radical procedures. In selected cases, nerve sparing type III/C1 and modified type II/B radical hysterectomies have resulted in reduced morbidity without detrimental effects in terms of survival outcomes, thus promoting the value of more tailored treatment strategies [1,4].

Similarly in recent years there has been growing interest in the literature toward the reliability of sentinel node (SLN) mapping in cervical cancer staging and in terms of its current clinical impact. In fact in early stage disease, SLN mapping could help surgeons to detect "key nodes" in atypical localizations, triaging of patients and shifting from systematic pelvic lymphadenectomy to SLN biopsy only, improving the detection of micrometastatic disease thanks to ultra staging processing of the SLN. According to the most recent series on cervical cancer, 75-88% of SLN are retrieved between the external iliac region and the obturator fossa [5-7]. Nevertheless, the paracervical lymphatic tissue is the primary site of extra uterine tumor spread: this is the mainstay to resect the parametria when performing radical hysterectomy [2,8].

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Complete pelvic lymphadenectomy does not include the systematic identification of parametrial lymph nodes, which in fact are usually found and described by the pathologist in the context of the parametrium [9]. Currently the prognostic significance of isolated and occult micrometastatic parametrial lymph nodes, especially if in association with an adequate number of negative pelvic nodes retrieved by systematic lymphadenectomy, is still unclear [2,3]. It also remains unclear whether these small lymph nodes should be searched for and separately isolated. Indeed, due to their small volume, parametrial lymph nodes might be difficult to identify. The recent technical development and introduction of high-definition cameras, such as the one fitted on the da Vinci® surgical system (Intuitive Surgical, Inc., Sunnyvale, CA) could provide a breakthrough technique. With this video (video 1) we aimed to show the identification of the SLN through robotic and standard colorimetric lymphatic mapping during a comprehensive surgical staging for an early stage cervical cancer.

Robotic parametrial Sentinel nodal mapping video: *https://www.youtube.com/watch?v=zS_k9BkJ0rU*

Materials and Methods

In our Department robotic surgery represents the first treatment option for cervical and endometrial cancer. Detailed description of surgical procedures has been previously reported [10,11].

Surgery was performed under general anesthesia with the patient placed in modified dorsal lithotomy position with Allen hydraulic stirrups with the legs abducted and with hip extension to accommodate the second assistant surgeon and the robotic surgical cart between the patient's legs, with both arms tucked comfortably. Patient received a mechanical bowel preparation, short term intravenous antibiotic prophylaxis with cefazoline, compression stockings and low-molecular-weight heparin for deep venous thrombosis prophylaxis.

After induction of general anesthesia, immediately before the insertion of the uterine manipulator (RUMI System®, Cooper Surgical, Trumbull, CT), we proceeded with intraoperative lymphatic mapping: a 1% solution of methylene blue dye was injected under direct visualization at the 3 O'clock and 9 O'clock sites of the cervix using a 25-gauge needle with no blood return prior to injection. One mL of methylene blue dye was injected deeply and 1 ml was injected superficially, for a total of 4 ml [7,12].

A total of four ports were used: a 12-mm camera port was placed into the umbilicus using the open-Hasson technique. Intra-abdominal pressure was maintained at 12 mmHg. Two 8-mm ancillary robotic trocars were placed bilaterally under direct vision, approximately one handbreadth away from the camera port to prevent collision between robotic arms. An ancillary 12-mm trocar was placed in the left subcostal area to be used by the assistant surgeon (for retraction, introduction of vascular clips, suction/irrigation). After the introduction of the trocars the patient was placed in steep Trendelenburg position. After a 360° inspection of the abdominal cavity, reduction of the bowel into the upper abdominal quadrants and peritoneal cytology sampling the da Vinci S surgical system (Intuitive Surgical, Sunnyvale, CA, USA) was then docked. The robotic equipment included the EndoWrist PK grasper (RG-PK Gyrus ACMI, Maple Grove, MN), the EndoWrist Fenestreted Bipolar Forceps and the EndoWrist Monopolar Curved Scissors Hot Shears.

While deviating the uterus to the left side, dissection began on the right side, about 10 minutes after blue dye injection. The superior and anterior leaves of the broad ligament were developed together with the dissection of the round ligament at its emergence in order to expose the iliac vessels and the ureter. Next the pararectal and paravescical spaces were developed: it is crucial to proceed with meticulous hemostasis as even a minimal bleeding in the reticular connective tissue may obscure the blue lymphatic channels.

The right uterine artery was then isolated at its emergence in order to identify the lateral parametrium and the first blue-labeled lymphatic channels. When more than one lymph node was observed on one side, the closest node to the cervix and parametrial lymphatic pathway was considered "first" SLN.

By following and dissecting these small vessels, a first SLN medial to the external iliac vein was identified and dissected. A second SLN was retrieved among the superficial obturator nodes. We the proceeded on to the left side, developing the retro peritoneum as

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formerly described. On the left the lateral lymphatic trunk [13] was more evident together with a first parametrial SLN which was separately isolated. The dissection proceeded with the identification of another two SLN in the interiliac region.

SLN were marked with clips and removed with endobags separately on each side. These specimens underwent ultra staging in agreement with previous studies [8,9]. No frozen sections were performed on SLN specimens in order to completely preserve pathology.

After proceeding with bilateral SLN mapping, we performed a modified type II/B2 radical hysterectomy with bilateral salpingo-oophorectomy with level 1 and level 2 pelvic lymphadenectomy according to the Querleu-Morrow classification [4].

The surgical procedure and post-operative period were uneventful. The patient was discharged on post-operative day two. The final pathologic examination confirmed the diagnosis. After multidisciplinary consultation between the Departments of Gynecology, Oncology, Radiotherapy, Pathology and Radiology, no adjuvant therapies were deemed necessary.

Discussion

Since the introduction of SLN mapping, many efforts have been made to provide a standardization of pelvic lymphadenectomy technique and nomenclature, and a more precise and reliable description of the pelvic lymphatic pathways [2,9].

The presence of several independent bilateral lymphatic channels draining from the cervix had already been observed by Reiffenstuhl more than fifty years ago, particularly the lateral, anterior and posterior trunks, thus supporting the evidence of multiple SLN [2,3,5,13].

However, the most frequent site of spread from cervical cancer is the lateral parametria, mainly due to tumour emboli in the lymphovascular spaces and in the parametrial nodes through the lateral lymphatic trunk [3,13]. In particular in 2000 Benedetti-Panici and colleagues found a parametrial node in more than 90% of the analyzed specimens of 69 cervical cancer patients, suggesting therefore that these nodes are present in almost all women. In addition they found in 100% of cases with positive pelvic nodes some evidence of parametrial involvement and cases of parametrial metastases without pelvic nodal involvement, thus confirming that the parametria are the first target of tumor spread [3].

In a series of dissections performed on 18 injected fresh cadavers Ercoli and colleagues confirmed the presence of three main lymphatic pathways: the most relevant was the "supraureteral paracervical pathway", limited cranially by the peritoneum and caudally by the ureter and draining into the interiliac, external iliac and common iliac lymph nodes, which was documented in 96% of specimens, representing the exclusive cervical drainage in 70% of cases [2].

Despite these anatomical conditions the vast majority of SLN are retrieved in the interiliac regions [5,9] whereas the prevalence of parametrial SLN is less than 15% [5,14]. The reason for this difference between theoretical and practical findings might be of a technical nature. Indeed, Frumovitz and colleagues reported that, using a "triple injection" with blue dye, radiocolloid and India ink, as a confirmation tool, they were able to identify parametrial nodes as SLN in 87% of women who had parametrial nodes [8].

In this regard SLN labeling with blue dye should be preferred [5]. Indeed the high concentration of radio-colloids in the cervix may lead to the under detection of neighboring SLN in the parametria. Similarly, as also highlighted in our video, following the lymphatic vessels is crucial to identify the small parametrial nodes. Standard colorimetric technique with blue dye could provide better assistance during retroperitoneal dissection compared to the use of indocyanine green and endoscopic near-infrared fluorescence imaging, avoiding frequent switching back and forth from near-infrared to white light [12,15].

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By contrast, the use of near-infrared technology with indocyanine green seems to provide excellent detection rate of SLN. A combination of both of these tracers might be of use for a better understanding of this issue. It should also be stressed that the advantages given by the robotic system could be of particular interest in this setting, thanks to the enhanced view given by the 3D high definition camera combined with motion scaling for a more gentle and precise retroperitoneal dissection. In addition, the brand-new Da Vinci Xi system Intuitive Surgical, Sunnyvale, CA, USA is provided with an already built-in near-infrared fluorescence imaging called Firefly camera in order to enhance these applications [16].

Conclusion

In conclusion we feel that SLN mapping will soon represent the standard of care for selected early stage cervical cancer. However we need also to clarify whether or not the parametrial nodes are the true SLN and what their prognostic role may be. We hope that this video may contribute to encourage discussion toward this still unanswered question.

Conflicts of Interest

Drs. G. Siesto F Romano and D Vitobello have no conflicts of interest or financial ties to disclose.

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