Laparoscopically-assisted intraoperative lymphatic mapping in endometrial cancer: preliminary results

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Summary

Objective: To analyse the results of a pilot study and determine the contribution of laparoscopically-assisted lymphatic mapping in patients with endometrial cancer.

Methods and Materials: In eight cases of early endometrial cancer, patent blue –V was injected laparoscopically into the uterine wall during a surgical staging procedure.

Results: A deposition of the blue dye was found in at least one pelvic lymph node in five of eight cases. Blue-colored nodes were observed in a total of 11 lymph nodes. Locations of these nodes included obturator, internal and common iliac sites. Only one blue colored node was positive for disease. An average of 15 lymph nodes were removed in the study group (range, 12-22). Uterine lymphatic vessels with bilateral drainage to the broad and infundibulopelvic ligaments were seen in all cases within 30-60 seconds.

Conclusion: Our initial experience with laparoscopically-assisted lymphatic mapping confirmed that the use of a minimally invasive technique is feasible. Lymphatic channels in the pelvic areas were seen in every patient. A deposition of blue dye in laparoscopically identifiable lymph nodes was seen only in 62.5% of patients. However, we believe that the lymphatic mapping of the uterine corpus can improve the accuracy of surgical staging in patients with endometrial cancer.

Key words: Laparoscopy; Lymphatic mapping; Endometrial cancer.

Introduction

One of the cornerstones of gynecologic cancer surgery is the assessment and removal of the regional lymph nodes. The significance of pelvic and para-aortic lymph node involment has been documented [1]. The presence of lymph node metastases has a major impact on the prognosis of women with endometrial cancer. Laparoscopically-assisted surgical staging (LASS) of endometrial cancer is a recently reported operative technique [2]. Identification of lymph node metastases is an integral part of surgical staging. However, the most appropropiate and realiable technique for assessing regional pelvic and paraaortic nodes remains uncertain [3]. Intraoperative lymphatic mapping and sentinel lymph node dissection (SLND) were, therefore, designed as a minimally invasive alternative to routine elective lymph node dissection in patients with early-stage cutaneous melanoma [4]. The sentinel node (SN) is the first lymph node to receive cancer cells metatasizing from the primary tumor.

Burke and colleagues [3] reported in 1996 the open technique of intra-abdominal lymphatic mapping to direct selective pelvic and paraaortic lymphadenectomies in women with high risk endometrial cancer. Since this initial pilot study on open intra-abdominal lymphatic mappping in endometrial cancer, only a few reports of cases of vulvar and cervical cancer undergoing this procedure have been published [5-8]. We report the results of our pilot study using a minimally invasive surgical technique of lymphatic mapping in laparoscopically treated patients with endometrial cancer.

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Subjects and methods

Eight patients underwent laparoscopically-assisted lymphatic mapping (LALM) and other gynaecological staging procedures for early-stage endometrial cancer between February and November 2000. Ages of of the patients ranged from 48 to 68 years, with a mean of 58.5. Patient weight ranged from 61 to 100 kg, with a mean of 81.2 kg: half weighed over 81.7 kg (180 pounds). Preoperatively, all patients underwent a complete history and physical examination, and routine laboratory investigation included biopsy, ultrasound, computed tomography or magnetic resonance. The patients were selected consecutively and criteria for a laparoscopic approach included a clinician's suspicion of early stage endometrial cancer (grade 2 or 3) and myoinvasion as well as a mobile uterus amenable to a laparovaginal approach to hysterectomy. The decision concerning the extent of laparoscopic surgery was based on guidelines suggested by Childers (2). The study protocol was approved by the Regional Committee on Human Research at the Kladno hospital and participiants gave their informed consent upon enrollment. This study was supported by a Grant Fund from the Minister of Health.

Surgical technique

Laparoscopy, using video monitoring equipment, was carried out with the patients in the lithotomy position. The telescope was insterted at a subumbilical site and one 10 mm port of entry was made medially. Finally, two or three 5 mm ports were placed in each of the lower quadrants at the lateral edge of the rectus muscle. At the time of exploratory laparoscopy and after obtaining washings for cytologic examination, the fallopian tubes were occluded by laparosonic coagulation. The intraoperative mapping technique for an open procedure described by Burke *et al.* [3] was modified for laparoscopy. Two milliliters of patent blue-V (2.5% in adequeous solution containing 0.6%

of sodium chloride and 0.05% of disodium hydrogen phosphate (Laboratoire Guerbet, Aulney-Sous-Bois, France) were injected into the subserosal myometrium at three midline sites using a 5 mm laparoscopic puncture needle with a 1.2 mm wide needle bore on the end (Karl Storz Endoscope, Tuttlingen, Germany). Injection sites were at the most superior portion of the uterine fundus, the anterior midline 2 cm below the superior injection site, and the posterior midline 2 cm below the superior injection site. The injection sites were selected to mimic a location of endometrial cancer arising in any part of the uterine corpus. Midline injections were used to maximize chances of observing bilateral pelvic lymphatic drainage. Dye uptake was monitored transperitoneally for five minutes after injection and then, the pelvic retroperitoneal spaces were opened. The laparoscopic technique for pelvic lymphadenectomy (PLN) has been described in a previous study [9]. The upper limit for a pelvic lymph node disssection was situated at the level of bifurcation of the common iliac vessel while the lower limit for PLN was the femoral ring and the pelvic floor. A lymph node nomenclature followed the anatomical and surgical criteria previously described [10]. Pelvic groups included the common iliac, external iliac, obturator, internal iliac, and presacral nodes. All the lympho-adipose tissue surrrounding the pelvic vessels was excised. Blue lymphatic channels were dissected in an effort to identify dye-containing lymph nodes in the pelvic regions. When identified, these nodes were removed as biopsies and forwarded to pathology as individual specimens. The nodal package was removed from the operative field through the upper 10 mm trocar. After the pelvic lymph node dissection, a laparoscopically-assisted vaginal hysterectomy and bilateral salpingo-oophorectomy was carried out.

A harmonic scalpel and laparosonic coagulating shears (LCS-K5), (Ultracision, Ethicon Endo Surgery, Johnson&Johnson Ltd, Cincinnati, Ohio, USA) were used in most cases, whereas, bipolar electrocauters (Karl Storz Endoscope, Tuttlingen, Germany) were applied in some cases only.

Results

The results are summarised in Table 1. Adenocarcinoma was the most common histology found in the study group. One patient had grade 1, four had grade 2 and two had grade 3 endometrial adenocarcinomas, and two patients had grade 2 adenoacanthomas. A deposition of dye into at least one lymph node was found in five out of eight cases (62.5%). Even though no deposition of the dye in the sentinel nodes took place in two patients, markedly enlarged tortuous lymph vessels were found, which led to lymph nodes larger than 10 mm. Using a microscope, a focal hyperplasia of the lymphatic sinus reticuloendothelium was found. An uptake of the dye was observed in a total of 11 lymph nodes. The mean number of blue-colored sentinel nodes was two (range: 1-3). Locations of these nodes included obturator and internal iliac sites in nine and common iliac in two. One woman (12.5%) was found to have cancer within two resected obturator nodes, but only one lymph node was marked by blue dye. On the whole, 120 lymph nodes were removed. The average number of removed lymph nodes in our group was 15 (range 12-22). Uterine lymphatic vessels with bilateral drainage to the broad and infundibulopelvic ligaments were seen in all cases within 30-60 seconds. The dye within the lymphatic channels was easily seen after the round ligaments were divided and lateral pelvic incisions were made to expose retroperitoneal structures. In some cases, dissection along the sprayed larger lymphatic vessels led to an evident blue-stained lymph node. Even in cases of uncolored nodes, a dissection along colored lymphatic vessels allowed for identificaton of a range of lymphatic pelvic nodes.

Table 1. — *Outcomes and histo-pathological findings.*

No	Patient stage	grade	LN (n)	DCLN (n)	Specimen (g)	blood loss (ml)	time of surgery (min)
1	Ic	2	12	0	140	50	150
2	Ia	2	12	0	120	150	120
3	IIIc	3	18	2	100	170	150
4	Ib	2	15	1	140	50	120
5	Ib	3	17	3	80	180	170
6	Ib	2	22	3	200	200	135
7	Ib	1	12	2	130	50	120
8	Ib	2	12	0	80	50	120

Abbreviation: n=number; LN=lymph node; DCLN=dye-containing lymph node.

The average time of surgery was 134.38 min (range 120-170). The laparoscopic injection technique added about 10 minutes to the surgical time compared with usual times for complete pelvic lymphadenectomy. Blood loss was minimal and no transfusion was required. No intraoperative or postoperative complications were observed. Hospital stay varied between three to four days. No adverse reactions were attributed to dye injection.

Discussion

The presence of regional lymph node metastases is an important prognostic factor for most solid neoplasms. Complete lymph node dissection (CLND) is considered the gold standard for staging patients. However, this technique is of questionable therapeutic value and is associated with considerable morbidity [11]. In 1990, Morton *et al.* [4] introduced intraoperative lymphatic mapping and sentinel node dissection as an alternative to CLND in patients with early-stage melanoma. The selective lymph node dissection evolved from the hypothesis that a primary melanoma metastazing via the lymphatics would lodge in the sentinel nodes excised before spreading to other nodes further along the lymphatic chain. The tumor status of the sentinel node excised during SLND determines the tumor status of the basin. In an initial study by Bilchik *et al.* [11], a sentinel node was identified in 82% of lymph node basins using blue dye alone without preoperative lymphoscintigraphy. More recently, the abovementioned authors reported that sentinel nodes were successfully identified in 98% of patients with the use of intraoperative lymphoscintigraphy. These data demonstrate that the sentinel node hypothesis applies to all solid neoplasms. After establishing SLND using blue dye alone in melanoma patients, the technique has been applied to breast cancer and to other solid tumors such as thyroid cancer, Merkel cell tumors and squamous cell carcinoma of the head and neck [12-15]. Dye-directed SLND has recently been reported for gastrointestinal and

gynaecological malignancies [12, 16]. Saha *et al.* [16] found that a histopathological examination of the sentinel nodes accurately predicted nodal metastasis in 94% of patients with colon cancer. Similar studies have shown feasibility of SLND using blue dye alone in vulvar, cervical and endometrial cancer [3, 5-8]. In a small pilot study, Medl *et al.* [7] demonstrated that preoperative lymphatic mapping is an easily performed technique to visualise SLND in cervical cancer. A rare pilot study is one performed by Burke *et al.* [3] in 1996 in which the authors explored the possibility of using open intra-abdominal lymphatic mapping as a method to visualize the lymphatic drainage of the uterus. This study reported a number of interesting findings. A deposition of isosulfan blue dye into at least one of the lymph nodes was only observed in 67% of cases. No blue para-aortic nodes were identified below the level of the origin of the inferior mesenteric artery. This would suggest that the para-aortic lymphatic channel from the uterus parallel to the ovarian vessels and lymph node biopsies from the lower aorta do not reflect drainage from the uterus.

In our pilot laparoscopy study, we used an identical technique of blue dye application. Contrary to the study of Burke *et al.* [3], we used a different type of the dye (patent blue-V) and an application needle with a wider diameter (1.2 mm). We were afraid to use a tuberculine needle because of a risk of breakage. Recently, Bostick and Giuliano [17] reported on the intralymphatic kinetics of various blue dyes. Methylene blue rapidly difused into surrounding tissues without staining the SN. Cyalume and flourescein stained the SN but required a dark room for visibility, otherwise its diffusion into the surrounding tissues made it difficult to distinguish the SN from surrounding lymph nodes, respectively. In contrast, patent blue-V and isosulfan blue rapidly entered the lymphatics after an intradermal injection with minimal diffusion into surrounding tissues. In a review article, Koop *et al.* [18] stated that the combination of blue dye and lymphoscintigraphy may be complementary for locating sentinel nodes.

The results of our preliminary study, in which a laparoscopic technique was used, confirmed a number of observations similar to those made during open mapping in the study of Burke *et. al.* [3]. Also, large-caliber lymphatic channels were often seen traversing the pelvic areas without leading into an identifiable node. Colored nodes were found in only five patients out of eight. The question is whether the wide variation in the location of pelvic nodes with dye uptake allows a sentinel nodal sampling in concrete pelvic regions to be performed. No dye deposition took place in larger lymphatic nodes with a reactive hyperplastic component, but centriperipetal lymphatic channels were markedly dilated and observation of their course made identification of the SN easier. Here, it is appropriate to ask what caused hyperplazy of the pelvic nodes and whether analogous changes existed with respect to the SN in the region of the axilla, skin, chest and gastrointestinal tract. In the patient with metastases in the nodes located in the fossa obturatoria region, only one lymph node was contaminated with the dye. It is not entirely clear whether a penetration of dye into other afflicted nodes takes place during a metastatic or hyperplastic affliction of a sentinel node.

Our initial experience with laparoscopically-assisted intraoperative mapping confirmed that the use of minimally invasive techniques is feasibile in patients with endometrial cancer. Lymphatic channels in pelvic areas were seen in every patient. A deposition of dye into laparoscopically identifiable lymph nodes was seen only in 62.5% of cases. However, we believe that the lymphatic mapping of the uterine corpus can improve the accuracy of surgical staging in patients with uterine malignancy. The fundamental question is whether the concept of lymphatic mapping as originally proposed by Morton *et al.* [4] can be applied to endometrical cancer. Further extensive prospective studies have to be carried out to confirm whether a needle technique, which we used, and selected dye and application sites reflect the true lymphatic drainage of the endometrial cancer and whether spreading of the blue dye into a pelvic lymphatic stream will make identification and removal of sentinel pelvic lymphatic nodes from defined regions easier.

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