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Sentinel lymph node biopsy in endometrial cancer—Feasibility, safety and lymphatic complications

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HIGHLIGHTS

- Sentinel node biopsy had a 14-fold decreased risk of lower extremity lymphedema.
- Sentinel node biopsy per se was not associated with intraoperative complications.
- Sentinel node removal in low-risk endometrial cancer is feasible and safe.

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ABSTRACT

Objective. To compare the rate of lymphatic complications in women with endometrial cancer undergoing sentinel lymph node biopsy versus a full pelvic and infrarenal paraaortic lymphadenectomy, and to examine the overall feasibility and safety of the former.

Methods. A prospective study of 188 patients with endometrial cancer planned for robotic surgery. Indocyanine green was used to identify the sentinel lymph nodes. In low-risk patients the lymphadenectomy was restricted to removal of sentinel lymph nodes whereas in high-risk patients also a full lymphadenectomy was performed. The impact of the extent of the lymphadenectomy on the rate of complications was evaluated.

Results. The bilateral detection rate of sentinel lymph nodes was 96% after cervical tracer injection. No intraoperative complication was associated with the sentinel lymph node biopsy per se. Compared with hysterectomy alone, the additional average operative time for removal of sentinel lymph nodes was 33 min whereas 91 min were saved compared with a full pelvic and paraaortic lymphadenectomy. Sentinel lymph node biopsy alone resulted in a lower incidence of leg lymphedema than infrarenal paraaortic and pelvic lymphadenectomy (1.3% vs 18.1%, $p = 0.0003$).

Conclusion. The high feasibility, the absence of intraoperative complications and the low risk of lymphatic complications supports implementing detection of sentinel lymph nodes in low-risk endometrial cancer patients. Given that available preliminary data on sensitivity and false negative rates in high-risk patients are confirmed in further studies, we also believe that the reduction in lymphatic complications and operative time strongly motivates the sentinel lymph node concept in high-risk endometrial cancer.

1. Introduction

Although lymph node status is an important prognostic factor in endometrial cancer the clinical significance of a full pelvic and paraaortic lymphadenectomy has yet to be established [1–5]. A sentinel lymph node procedure is an intermediate between a full versus no lymphadenectomy [6–10]. Reduced perioperative morbidity and lymphatic complications associated with a full staging procedure and detection of lymph node metastases in low-risk, as well as preoperatively erroneously understaged patients, are proposed advantages of a sentinel lymph node concept [7,11–13]. In addition, ultrasectioning and immunohistochemistry evaluation that is logistically and economically feasible only for a limited number of lymph nodes, increase the rate of metastasis detection [12]. Although less extensive than a full lymphadenectomy, a sentinel lymph node dissection and removal can mean an increased perioperative risk, longer operative time and lymphatic complications in low-risk women traditionally not subjected to lymph node dissection.

Lymphatic complications after treatment for gynecologic cancer substantially impact the patients' quality of life [14–16]. Lower extremity lymphedema with an incidence of 3.7%–47% is the most common lymphatic complication after gynecologic cancer treatment followed

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by lymphoceles which are reported in up to 27% of patients [14–21]. The occurrence of truncal lymphedema and lymphatic ascites is less extensively reported [22–25].

The incidence of lower extremity lymphedema is significantly lower after sentinel lymph node biopsy in cervical cancer than after systematic lymphadenectomy [26]. However, despite an increasing use of sentinel lymph node biopsy in endometrial cancer, the incidence and potential reduction of lymphatic complications following removal of sentinel lymph nodes only compared with a full lymphadenectomy remains unknown.

The Department of Obstetrics and Gynecology at Skåne University Hospital, Lund, Sweden is a tertiary referral center for malignant gynecological surgery. Robotic surgery using the da Vinci® surgical system (Intuitive Surgical Inc., Sunnyvale, Ca, USA) has been utilized since 2005, and is the surgical method of choice for women with endometrial cancer unless contraindicated by uterine size, suspect disseminated disease, or anesthesiological reasons.

The aims of this study were to compare the rate of lymphatic complications in women with endometrial cancer undergoing sentinel lymph node biopsy versus sentinel lymph node biopsy followed by a full pelvic and infrarenal paraaortic lymphadenectomy, and to examine the overall feasibility and safety of the former.

2. Material and methods

Women with endometrial cancer scheduled for robotic surgery between June 2014 and September 2016 were offered participation in this study. All included women gave their written, informed consent.

Prior to surgery, all women underwent a computer tomography (CT) of the thorax and abdomen, as well as an expert transvaginal ultrasonography to assess myometrial and cervical invasion. Women with high-risk endometrial cancer (either one of non-endometrioid histology, FIGO grade 3, non-diploid flow cytometry, myometrial invasion >50% or cervical invasion) were scheduled for a complete pelvic and infrarenal paraaortic lymphadenectomy after an initial separate removal of sentinel lymph nodes. In addition, an infracolic omentectomy was performed in cases of a non-endometrioid histology. A limited procedure (a paraaortic lymphadenectomy restricted to the level of the inferior mesenteric artery, a full pelvic lymphadenectomy without paraaortic dissection, or a sentinel lymph node biopsy only) was planned upfront in case of extensive comorbidity or advanced age. Patients without any high-risk factors were allocated to sentinel lymph node biopsy.

Indocyanine green (ICG) was injected either in the cervix or the fundus, for the latter a transabdominal injection using a Williams Cystoscopic Injection needle (Cook Incorporated, Blimington, USA) was performed. Sentinel lymph nodes were strictly defined according to a previously described anatomically based surgical algorithm, with the aim of bilateral identification of sentinel lymph nodes along both the upper and lower paracervical pathways (Fig. 1) [9,13]. The uterine pelvic lymphatic drainage follows two major pathways. The upper paracervical pathway runs along the uterine artery to the medial external iliac and obturator nodes, continuing lateral to the common iliac artery to the paraaortic nodes. The lower paracervical pathway runs medial to the internal iliac artery to the presacral nodes and continues medial of the common iliac artery to the paraaortic area. The surgical technique has been described previously [9,13]. In case of one or more unidentified lymphatic pathways, mostly the lower paracervical pathway, a submucosal cervical ipsilateral reinjection of ICG was performed.

Patients with stage one endometrioid adenocarcinoma with a maximum of one risk factor (FIGO grade 3, non-diploid flow cytometry, or myometrial invasion >50%) received no adjuvant treatment. Patients with endometrioid adenocarcinoma and two risk factors, or non-endometrioid endometrial cancer, but without lymph node metastases, received four cycles of carboplatin and taxanes as did stage II and III patients. Stage II and III patients also received 46 Gy external radiotherapy to the pelvis and when indicated, to the paraaortic area. Patients with cervical/vaginal engagement were additionally treated with 10 Gy of brachytherapy. Age or comorbidity limited adjuvant treatment in some patients.

Baseline demographics, perioperative and follow up data were prospectively collected for all patients. To estimate the duration of the sentinel lymph node procedure, the surgical times for women undergoing sentinel lymph node biopsy were compared to women undergoing

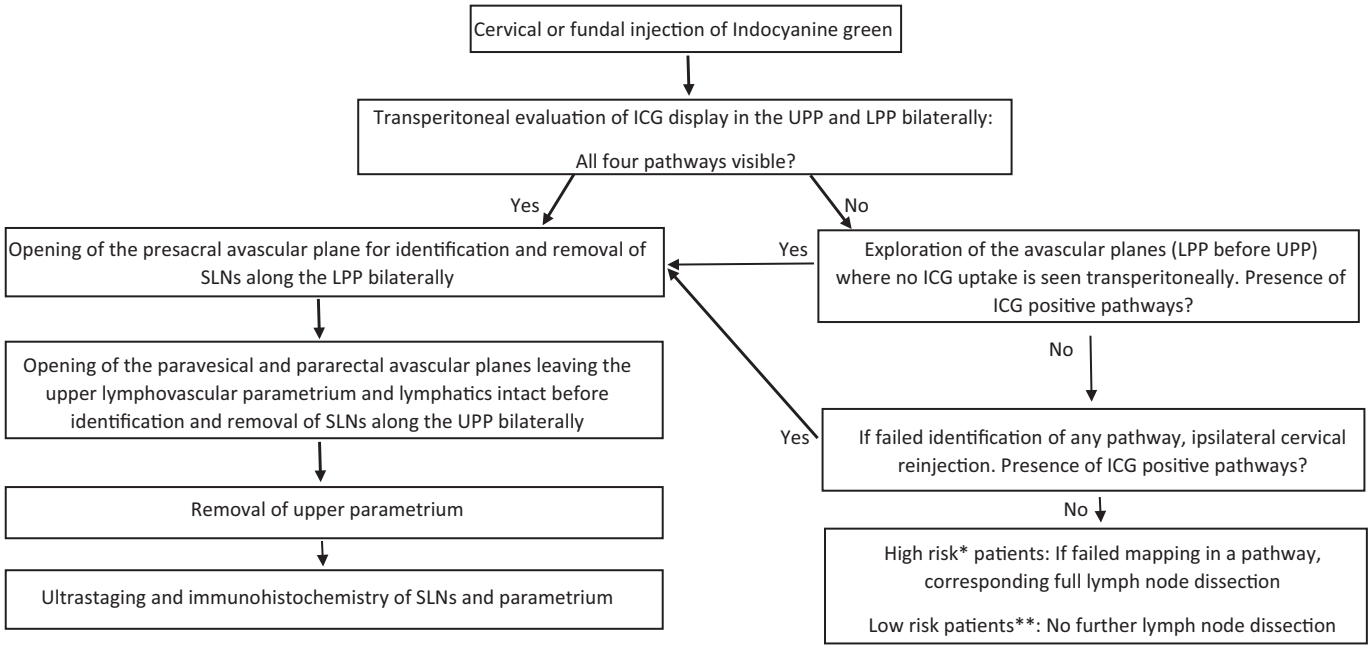

Fig. 1. Surgical algorithm for identification of sentinel lymph nodes (SLNs) in endometrial cancer. ICG = Indocyanine green, UPP = Upper paracervical pathway, LPP = Lower paracervical pathway. SLN type 1: ICG positive juxtauterine colored lymph node in each pathway. SLN type 2: ICG negative lymph node closest to the uterus with a clear afferent lymph vessel in the absence of ipsilateral colored nodes. SLN macro: any macroscopically suspicious lymph node. If failed mapping in a pathway: lymph node dissection along this pathway. * at least one of following risk factors: FIGO grade 3, non-endometrioid histology, non-diploid flow cytometry, myometrial invasion >50%, cervical invasion, ** no risk factor.

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