Editorial

Sentinel lymph node mapping in endometrial cancer: time for a change

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How J, Gauthier C, Abitbol J, *et al.* Impact of sentinel lymph node mapping on recurrence patterns in endometrial cancer. Gynecol Oncol 2017;144:503-9.

How J, Boldeanu I, Lau S, *et al.* Unexpected locations of sentinel lymph nodes in endometrial cancer. Gynecol Oncol 2017;147:18-23.

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Since the publication of the results of the clinic-pathological study GOG #33, staging for endometrial cancer changed from clinical to surgical and required a pelvic and para-aortic lymphadenectomy (1,2). Since then, the role of the pelvic and para-aortic lymphadenectomy has been widely debated. In patients with non-bulky lymph nodes, the lymphadenectomy plays a staging role. Since the risk of lymph nodal metastases varies in endometrial cancer patients and is particularly low in patients with small, well differentiated and superficially invasive lesions, several authors believe that the routine performance of a full pelvic and para-aortic lymphadenectomy is not useful and should be avoided in a specific subgroup of endometrial cancer patients (3).

A widespread approach to this problem is the performance of the full lymphadenectomy based on the identification of intrauterine risk factor at frozen section analysis. However, the performance of this strategy varies widely among institutions and depends on the threshold set for the indication to a full lymphadenectomy (4-8).

In the last few years, the sentinel lymph node (SLN) mapping has been widely adopted as an alternative to a conventional surgical staging. This approach may offer several advantages over a systematic lymphadenectomy, not only by reducing the surgical morbidity but also by increasing the precision of the lymph nodal information obtained. When talking about the SLN mapping in endometrial cancer it has to be kept in mind that this procedure is accepted as an alternative to a full lymphadenectomy only by part of the international guidelines (9,10).

Here, we will present three manuscripts that will help us discuss the clinical applicability of the SLN mapping in endometrial cancer first and the technical aspects of the mapping next. In the first manuscript, How *et al.* analysed the anatomic distribution of the SLNs in early stage endometrial cancer patients (11). In their series, 7.9% of the SLNs found in 13.1% of the cases were detected in areas, such as the parametria, the internal iliac vein and the pre-sacral area, that are not routinely included in the landmarks of a systematic lymphadenectomy. These results are consistent with those of other series in this setting (12,13). Anatomic studies have shown that the lymphatic drainage of the uterus is relatively complex. Two lymphatic pathways have been described: the first one, called upper paracervical pathway, drains to the lymph nodes located in the obturator fossa and the external iliac vessels, and a second one, called lower paracervical pathway, that drains to the pre-sacral lymph nodes (14). Whereas the lymph nodes draining the first pathway are included in the landmarks that define a systematic pelvic lymphadenectomy, the second ones

are not. Hence, through a systematic lymphadenectomy, we systematically omit to sample relevant lymph nodes. Interestingly, Persson *et al.* were able to show that in order to identify both lymphatic pathways bilaterally, a higher dose of tracer is needed (14). The definition of the optimal dose of tracer to be injected and the optimal number of SLNs that need to be retrieved is a still debated issue (15,16). Overall, the SLN mapping in endometrial cancer has proven to be reliable with a reasonable false negative rate, especially if the SLN mapping algorithm as proposed by the Memorial Sloan Kettering Cancer Center is applied (17).

In addition to the fact that the SLNs represent a targeted sampling, they also undergo a more thorough pathological analysis, the ultrastaging, that enables to identify small metastases that might have otherwise been missed. Through the SLN mapping we transition from a labour intense surgical procedure to a target surgical procedure and a labour intense pathological analysis.

The second manuscript addresses the impact of the SLN mapping on recurrence patterns in endometrial cancer (18). In a large retrospective study, How *et al.* compare disease free survival as well as pattern of recurrences in endometrial cancer patients treated with hysterectomy, bilateral salpingo-oophorectomy and systematic lymphadenectomy or SLN mapping followed by systematic lymphadenectomy. The authors could not find any differences in terms of disease-free survival at 48 months of follow-up but were able to show that in the group undergoing SLN mapping followed by systematic lymphadenectomy the pelvic side wall recurrences accounted for a significantly less common. The authors conclude that this may be the result of a more efficient detection of the SLNs enabling for a more meticulous removal of affected lymph nodes.

Other institutions have compared disease free and overall survival among patients undergoing a systematic lymphadenectomy or a SLN mapping further proving the oncological safety of the SLN mapping as compared to a full lymphadenectomy both in low risk and in high risk endometrial cancer patients (19-21). In high intermediate risk endometrial cancer patients, overall survival is negatively affected if pathological lymph nodal data are lacking (22). Both patients with pathologically non-affected and affected lymph nodes have better survival curves as compared to patients who had not been surgically staged (22). These data clearly show that the prognostic value of the pathological lymph nodal status, at least in this subgroup of patients, is of great importance and helps directing appropriate adjuvant treatments.

Finally, we want to discuss the technical aspects of the SLN mapping. When performing a SLN mapping various tracers with different performances can be adopted: Tc-99m, blue dyes and indocyanine green (ICG) (23). In a prospective trial, How *et al.* injected 100 endometrial cancer patients intracervically with the three tracers and evaluated the performance of the tracers in terms of detection rates (24). In their analysis, the use of blue dye did not seem to increase the detection rates of the cocktail of traces and the authors recommend to use a combination of Tc-99m and ICG only. Since its application as a tracer for SLN mapping, ICG has become the preferred tracer because of its safety profile and user friendliness (22). Nowadays, ICG is mostly used alone and not in combination with other tracers, since it has repeatedly demonstrated to yield higher detection rates as compared to the conventional tracers (25,26).

Despite controversial indications of different international guidelines, SLN mapping is rapidly gaining acceptance in clinical practice. SLN mapping not only allows to reduce the surgical trauma and therefore the surgical morbidity but is a more precise and efficient method as compared to a systematic lymphadenectomy in identifying the most representative lymph nodes to be analysed under the microscope.

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