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Editorial

How to perform sentinel node detection in high-risk endometrial cancer: one step forward

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Endometrial cancer is the most common gynecologic cancer in developed countries. Its incidence is rising in several parts of the world, in parallel to the incidence of obesity. This concerns mainly low-risk lesions, most of them being cured by a total hysterectomy with bilateral salpingo-oophorectomy whereas high-risk tumors require more aggressive treatments [1].

The nodal staging of endometrial cancer is an old debate. No staging, limited pelvic dissection, pelvic and paraaortic dissection have been proposed according to clinical stage and time. The therapeutic value of nodal dissection has also been suggested. Unfortunately, trials addressing what we call now low and intermediate-risk endometrial cancers showed no benefit of a systematic lymphadenectomy [2].

Sentinel node biopsy (SLN) has been introduced more recently. This technique appears seductive since it could provide the nodal status with a limited surgical aggressiveness. The limitation of systematic extended dissections in routine was precisely the imbalance between the potential benefit in terms of staging and prognosis vs. the feasibility and the perioperative risk due to age and comorbidity. The interest to SLN is reinforced since it is usable by minimally invasive surgery, and more recently by the spread of indocyanine green with high accuracy [3].

Concerning endometrial cancer, 2 sites of injection are possible. The most used and evaluated is the cervix, with a technique similar to that of cervical cancer [3]. This approach is easy to learn, to practice, provides a good sensitivity and negative predictive value especially for low-risk or intermediate-risk tumors. However, cervical injection does not explore the lymphatic drainage of the tumor, and the rate of paraaortic SLN (and positive paraaortic nodes) is much lower than after classical dissections [4].

In this issue, Angeles et al. [5] report on a large experience of SLN with transvaginal myometrial injection. They included 102 patients with intermediate and high-risk endometrial carcinoma. All patients underwent SLN (isotope + blue dye) and pelvic + paraaortic dissection. The detection rate was 79%. The sensitivity and negative predictive value were 87.5% and 97%; and 83% and 96.9% for paraaortic metastases. This technique

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appears as effective as extended dissection to assess the nodal status of these patients, especially in the paraaortic area. However, the rate of isolated paraaortic SLN and moreover of positive isolated paraaortic SLN were low (respectively 6/81 and 3/20 patients). As in previous reports, most paraaortic involvement cases were associated to a pelvic spread. The technique presented in this paper is comparable to those previously described such as hysteroscopic injection, subserosal injection or dual injections. Moreover, it appears surprisingly well tolerated by the patients. We could argue that this technique makes realistic the search of rare isolated paraaortic metastases.

If the role of SLN in low risk and low-intermediate risk is now well established, its use in high intermediate and high risk is still controversial. Nonetheless, the recent ESGO/ESTRO/ESP guidelines for endometrial management state for SLN in this setting for lymph node staging in stage I and II, due to the high sensitivity to detect pelvic lymph node metastases and a high negative predictive value [1,6]. To be fully reliable in this context, the use of surgical SLN algorithm and experienced surgeons are mandatory.

The paucity of isolated paraaortic metastases is a question per se given that this event is rare (less than 2%). This may be explained by anatomic uterine lymphatic drainage pathway [7]. Usually, endometrial cancer spreads along the pelvic pathways. The lower and middle part of the uterus drain laterally to the parametria and then to the obturator lymph nodes, where are mostly found metastatic lymph nodes. The upper corpus and fundus drain to the interiliac lymph nodes, then to the common iliac lymph nodes and finally to the paraaortic lymph nodes. In very few cases, the fundic lymphatic drainage may reach directly to the paraaortic lymph nodes through the gonadal vessels and therefore shunt pelvic lymphatic drainage. Although the imaging (magnetic resonance imaging, positron emission tomography, or computed tomography scan) is not perfect, they permit to detect preoperatively paraaortic positive nodes with sufficient accuracy [8]. In addition, the ratio of the number of patients submitted to SLN vs. number of patients with improved prognosis due to the diagnosis and treatment of isolated aortic metastasis is questionable.

Finally, the real pending challenge is now to define the place of SLN at the light of the molecular classification [9]. The real impact of positive SLN for the adjuvant treatment is challenged by the molecular profile. Patients with POLE mutation have a negligible risk of nodal metastasis, an overall excellent prognosis and could avoid any nodal sampling. Patients with p53 mutations require mainly chemotherapy, whatever the result of nodal sampling. One could argue that positive paraaortic SLN could modify the radiation fields. We just emphasize that extended field radiation therapy has never proved any benefit in terms of overall survival. It could be hypothesized that SLN might provide an added prognostic value with diagnosis of micrometastasis and improve prognostic assessment of p53 mutated, or mismatch-repair deficient or mismatch-repair proficient patients. However, acceptable quality data are required in this subgroup before drawing such conclusion.

One of major concern is maybe first to standardize surgical techniques of SLN and to respect detection algorithm, as it could impact diagnostic accuracy and oncologic outcomes.

This paper makes things progress concerning the best approach to inject the tracer in endometrial cancer. It changes the vision of paraaortic nodal staging and keeps nodal surgery in the armamentarium of high-risk endometrial cancer. Future works have to correlate SLN and the molecular classification.

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