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Correspondence

Sentinel lymph node detection in endometrial cancer: hysteroscopic peritumoral versus cervical injection

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To the editor:

We read with great interest the article by Bogani et al. [1], highlighting some of the debated issues regarding the role of sentinel lymph node (SLN) mapping in endometrial cancer. However, taking a cue from this commentary and from the available evidence in the literature regarding the surgical staging of endometrial cancer, we would like to broaden the debate to include several important aspects not covered by the authors.

First of all, the authors state that even if hysteroscopic injection represents a more demanding and less reproducible technique, it is the more reliable and effective approach in detecting the lymphatic drainage of a tumor, whereas cervical injection seems to be more effective in detecting the lymphatic drainage of the uterus.

We disagree with that definition which sounds redundant and in contrast with the evidence the literature. In 1999, Linehan et al. [2] demonstrated that peritumoral intraparenchymatous SLN dye injection was not superior to intradermal dye injection in SLN detection of patients with breast cancer. In endometrial cancer patients one of the main criticisms regards cervical site injection and whether it map the organ rather than the tumor. In any case, the study of Khoury-Collado et al. [3] challenged the reservations about the effectiveness of cervical site injection, since after a cervical site injection, SLNs were three times more likely to harbor disease than non SLNs. More recently, Rossi et al. [4] confirmed that cervical injection of indocyanine green achieved a higher detection rate and a similar anatomic nodal distribution as hysteroscopic injection for SLN mapping in endometrial cancer patients. Furthermore, the rationale of using the cervix as injection site for SLN mapping has been confirmed by classic morphological studies. A well-known lymphatic pathway is composed of a complex network of bilaterally independent lymphatic channels, draining the uterine cervix and the corpus primarily from the lateral parametrial regions [5]. By applying the recently published SLN algorithm of the Memorial Sloan Kettering Cancer Center (MSKCC) [6] all the women with an apparently uterine-confined disease who undergo a cervical injection for mapping it is clearly stated that any suspicious nodes should be removed regardless of mapping.

From our point of view, hysteroscopic tracer injection includes some critical drawbacks: (1) the necessity for a more demanding technique with a longer learning curve compared to the cervical injection, requires the support of nuclear medicine when Tc99m is injected

JOURNAL OF GYNECOLOGIC ONCOLOGY

Table 1. Rate of isolated aortic nodal metastasis with negative pelvic lymph nodes in patients with endometrial cancer (published series with at least 100 cases)

Source	Year	Isolated aortic metastasis
Creasman et al. [9]*	1987	12/563 (2.1)
Morrow et al. [10]*	1991	18/802 (2.2)
Ayhan et al. [11]	1995	6/209 (3.0)
Onda et al. [12]	1997	2/173 (1.2)
Hirahatake et al. [13]	1997	2/160 (1.3)
Mariani et al. [14]	2004	5/229 (2.2)
Nomura et al. [15]	2006	4/105 (3.8)
Tanaka et al. [16]	2006	1/101 (1)
Mariani et al. [17]	2008	9/265 (3.4)
Hoekstra et al. [18]	2009	7/1,487 (0.5)
Lee et al. [19]	2009	7/284 (2.5)
Fujimoto et al. [20]	2009	7/313 (2.2)
Abu-Rustum et al. [7]	2009	12/734 (1.6)
Chiang et al. [21]	2011	2/156 (1.3)
Dogan et al. [22]	2012	2/145 (1.4)
Milam et al. [23]*	2012	12/532 (2.2)
Total		108/6,258 (1.7)

Values are presented as number/total number (%).
*Gynecologic Oncology Group Study.

with the patient still awake during the procedure; (2) if we can say that a tracer injection via hysteroscopy its preferable in the case of focal endometrial lesion, when the tumor fills the majority of the uterine cavity, it's not easy to decide where to inject the dye in respect of the hypothesis that hysteroscopic injection "is effective in detecting lymphatic drainage of the tumor"; and (3) considering that the exclusive aortic migration can occur more frequently in the case of a fundal high grade tumor with a deep myometrial infiltration, is it really a commitment to standardize such a demanding technique for such a limited number of cases?

From our preliminary experience in this subset of select cases, and based on preoperative histology, the application of an integrated positron emission tomography/computed tomography/SLN algorithm [7] achieved excellent results. This strategy allows for staging of all cases and provides useful individualized information that may be a guide in deciding further therapy. Furthermore, the incidence of para-aortic metastasis in the presence of negative bilateral pelvic nodes in surgically staged endometrial cancer patients is 1% to 3% [8]. Considering the published series including more than 100 cases of endometrial cancer patients (6,858 evaluated patients), the overall rate of isolated aortic metastasis recorded was 1.7% (**Table 1**) [9-23]. Mariani et al. [24] already underlined the issue of a low incidence of isolated aortic metastasis in 2001 in a large series of endometrial cancer patients suggesting that the aortic involvement with a skipped pelvic route is probably a late and rare event.

Sentinel node mapping represents an acceptable valid approach for surgical staging of patients with apparently confined early stage endometrial cancer with normal-appearing nodes. Therefore, in the case of suspicious preoperative imaging or intraoperative findings, the nodes should be evaluated/biopsied as part of an extent-of-disease evaluation, consequently overriding the importance of SLN mapping. By applying a well-defined algorithm, the MSKCC group achieved a very low false-negative rate—likely below 5% [6]. Moreover, the detection of stage IIIC disease is high, particularly in the pelvis. In

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absence of bilateral mapping a side-specific lymphadenectomy including the iliac and obturator nodes should be performed and this approach has been recently included in the National Comprehensive Cancer Network (NCCN) guidelines [25]. The detection of a stage IIIC2 disease may be higher if routine para-aortic lymphadenectomy is incorporated but the survival advantage of systematic aortic dissection in stage IIIC cases remains to be determined through a prospective trial not yet available.

In our opinion, the cervical injection still remains the easiest and most reproducible way to perform SLN mapping but at the same time, hysteroscopy injection in well skilled hands represents a valid alternative.

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