Editorial Commentary

Sentinel node mapping for uterine cancer: is less always more

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Introduction

Radical hysterectomy with systematic pelvic lymphadenectomy represents the gold standard surgical approach to early stage cervical cancer.

During the last decades the community of the gynecologic oncologists has faced a progressive shift of the surgical approach toward less "aggressive" procedures in order to minimize as much as possible the morbidity following the radical surgery, without affecting the survival outcomes.

Therefore, across this timeline, surgeons and oncologist have been used to concepts like minimally invasive approach, modulation of radicality, nerve sparing procedures, and last but not least, sentinel node (SLN) mapping.

To date, the nodal status of cervical cancer represents the most important prognostic factor in apparently early stage conditions and it is the driver for further adjuvant therapies.

SLN mapping is now a popular option for the management of early uterine (endometrial and cervical) malignancies, as it is included in the National Comprehensive Cancer Network guidelines among the viable options (1) of staging.

During the assessment of the feasibility and efficacy of SLN mapping in these years, a lot of tracers have been studied, including colorimetric, radiometric, florescent tracers alone or in combination with each other, in order to improve the detection rate, and in particular the bilateral detection rate, which is the most important outcome the evaluate the feasibility and reproducibility of the technique.

The introduction of the indocyanine green (ICG) in SLN mapping has dramatically improved this procedure that become easily more reproducible and effective in the assessment of the nodal status of each pelvic side (2,3).

This fluorescent dye, combined with a near-infrared imaging technology, easily allows not only to detect the lymph nodes, but alto to design and follow the entire lymphatic drainage as to distinguish between the usual pattern of drainage into the interiliac region to the uncommon pattern which goes to the presacral and para-aortic region.

In 2018 the FILM trial demonstrated in a randomized fashion that the ICG performs better than the colorimetric tracers (isosulfan blue dye) alone or even in combination. In particular, regarding the bilateral detection rate, ICG definitely resulted into an almost 80% of bilateral mapping vs the 30% of the isosulfan blue (4).

Very recently, the Sweden group, has reported the results of a prospective trial of SLN mapping in cervical cancer entitled "Combining Indocyanine Green and Tc^{99}-nanocolloid does not increase the detection rate of sentinel lymph nodes in early stage cervical cancer compared to Indocyanine Green alone". In this study authors used the ICG and a radiotracer (TC^{99} – Radiocolloid) to map the SLN in patients addressed to surgery for cervical cancer. In case of tumor of FIGO Stage IA2, or greater, a full pelvic lymphadenectomy was also performed. All the procedures were managed by robotic approach (5).

In the sixty-five analyzed women, the bilateral mapping rate was 98.5% for ICG and 60% for Tc^{99} ($P<0.01$). The combination of the tracers did not increase the bilateral detection rate. Authors, that are experts in this procedure and that adopted a strict protocol (which is mandatory if someone wants to perform SLN mapping in safety), achieved almost the 100% of bilateral, mapping. Therefore, also in this case, ICG was confirmed as the better dye for

the SLN mapping and, probably, no other tracer could perform better. The reasons might go beyond the fact that the ICG is fluorescent and therefore easy to be found. Probably the ICG flows into the lymphatic channels better than other tracers and therefore it's more useful to map the lymphatic system (channels and lymph nodes) (6).

If this trial, on the one hand has further confirmed that SLN mapping in cervical cancer works and that ICG is the tracer of choice, on the other hand it contributes to enhance a nowadays paradox: indeed, following the results of the LACC study (7), a randomized trial on the surgical approach to cervical cancer, patients (and surgeons) should be aware that the survival outcomes of patients managed by minimally invasive surgery (including robotics) for cervical cancer are worse than the open counterpart. This inevitably discourage the use of minimally invasive surgery to manage the cervical cancer and therefore also the application of the SLN mapping. In addition, due to these results, the design of other randomized trials, that could overcome all the criticisms that the LACC trial have raised, is hard to be sustained also from the ethical point of view.

So the paradox is to have found a viable and effective alternative to a systematic pelvic lymphadenectomy which is the SLN mapping with ICG, but, until the International Societies will provide official guidelines about, we have to turn back to the beginning of the history of surgery of cervical cancer through an open approach as a result of prudence.

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