Sentinel node in cervical cancer: resistance to change?

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“The true meaning of things lies in trying to say the same things in other words.”

Charles Chaplin

“How many times have you read an article that concludes: more studies are needed?” With this question Michael Frumovitz, specialist in Gynecology Oncology from MD Anderson Cancer Center, starts the interesting editorial entitled Sentinel Lymph Node Biopsy for Cervical Cancer Patients – What’s It Gonna Take?, published in Gynecologic Oncology in January 2017. Certainly, the prolonged wait for acceptance of the sentinel node biopsy in cervical cancer, as a method of routine in the determination of nodal status, is still incomprehensible.

What is the evidence needed to make a new methodology permanently accepted? It is well known the long road that neoadjuvant chemotherapy and interval surgery had to go in advanced ovarian cancer, especially in North America, to be accepted as an alternative to the primary cytoreductive surgery. Even the publication of the EORTC study in 2010 and subsequently the CHORUS in 2015, two series with a high level of statistics evidence, managed to frankly consolidate this therapeutic choice. Ignace Vergote and cols exposed many of the necessary explanations in an editorial published in August of 2016, Neoadjuvant chemotherapy in advanced ovarian cancer: What kind of evidence is needed to convince US gynaecological oncologists?

For the last quarter of 2016, after the simultaneously publication in the journals Gynecologic Oncology and Journal of Clinical Oncology, of the guides titled: Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: Society of Gynecologic Oncology and American Society
of Clinical Oncology Clinical Practice Guideline, it can be said that two of the most influential scientific societies in America have finally given their approval to this modality of treatment.

Now, it is necessary to ask: How resistant to change are we, the oncology specialists? As Frumovitz explains in his editorial, sometimes seems that not only requires a robust evidence to support the new proposal, but this too be convincing or pleasant to specialists. He uses as example the low acceptance of the intraperitoneal chemotherapy in cancer of ovary in the USA, despite the impeccable studies that endorse an evident benefit in survival \(^7\). By contrast, he cites vulvar cancer, a disease where the use of sentinel node biopsy has been accepted broadly by gynecologists oncologists around the world, based on evidence given by a study of validation (GOG 173) \(^8\) and a prospective, observational study with a single arm population, as it was the GROINSS-V \(^9\).

Sentinel node biopsy of the cervix has shown, in a recent meta-analysis\(^10\), a high safety profile in terms of identification rates (93.4%), 96.9% sensitivity for hemipelvis studied and a 99.3% negative predictive value. In January 2017, Genevieve K. Lennox and Allan Covens publish the study: *Can sentinel lymph node biopsy replace pelvic lymphadenectomy for early cervical cancer?*\(^11\). This study, conducted in patients with stage IA-IB2 cervical cancer, was designed to compare recurrence-free survival and morbidity among 110 patients with negative sentinel node versus 1078 patients who underwent bilateral pelvic dissection and without nodal disease (N0). It was concluded that there were no significant differences in recurrence-free survival at 2 and 5 years (97% vs 95% and 93% vs 92%, respectively). Pelvic dissection was significantly associated with an increase in surgical time (2.8 vs 2.0 h, \(p <0.001\)), blood loss (500 cc vs 100 cc, \(p <0.001\)), need of transfusions (23% vs 0%, \(p <0.001\)) and postoperative infections (11% vs 0%, \(p = 0.001\)).

In his article Frumovitz comments: *Lennox and Covens estimate that a well-designed prospective, phase III, randomized study comparing the two approaches for survival (complete pelvic lymphadenectomy vs. sentinel lymph node only) would require 1400 patients. In today's environment of decreasing cervical cancer incidence (thankfully) and decreasing research funding (not so thankfully), a study of this size will never be completed.*

*But, do we need such a study?* The answer is no, confidently the coming years will be key to lymphatic mapping and the sentinel node biopsy, in the surgical treatment of early cervical cancer, to be accepted as a new standard of care. From at least two versions ago, the NCCN maintains this methodology with a level of evidence 2B and especially indicated in patients with tumors of 2 cm or less in diameter. Likewise, they recommend adhering to the algorithm of lymphatic mapping, by cervical injection, with the technique proposed by MSKCC and studying not only the sentinel nodes, but those increased volume or suspects, although they have not captured the vital dye or radiotracer. If not is identify nodes with these characteristics, the recommendation is the lymphatic dissection of the hemipelvis with mapping failed. As well Frumovitz concludes in its editorial: *More studies are not needed. Action is now what our patients need.*

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Adopting this new methodology will enable the reduction of the incidence of unnecessary pelvic lymphadenectomy, but very probably be considered in patients with tumors less than 2 cm and negative sentinels lymph nodes, the option to omit the parametrectomy and perform a extrafascial hysterectomy, given the low risk of parametrial infiltration in this subgroup of patients. Definitely, it is a profound change in the way of treating this pathology which a few years ago looked unthinkable.

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References