



Sentinel lymph node biopsy in ovarian cancer: more questions than certainties

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In this month's Lead Article, Augusti and colleagues describe their systematic review and meta-analysis aimed at evaluating the detection rate and diagnostic accuracy of sentinel lymph node biopsy mapping in patients with early stage ovarian cancer.¹ The study showed a 92% pooled detection rate and 100% negative predictive value of sentinel lymph node biopsy. In particular, the dual tracers, technetium-99 and indocyanine green, and dual site injection (utero-ovarian and infundibolo-pelvic ligament), gave optimal detection when injected before adnexectomy. The paper will represent a reference for future studies with well defined protocols. Regrettably, as the authors highlighted, small sample size, period of inclusion of the studies, and substantial clinical and technical heterogeneity prevented robust conclusions on the accuracy of sentinel lymph node biopsy in this population.

Some controversial issues raised were:

- ▶ About 15% of cases initially classified as early stage are upstaged due to lymph node involvement,² particularly in high grade serous histology (28%) compared with other subtypes (6%). This value stems from old studies lacking an ultrastaging protocol, possibly underestimating early stage positive node cases. The meta-analysis included 113 patients, theoretically giving approximately 17 positive nodes, not 12 as reported. A 5% disparity could arise from inclusion of different histotypes and grades as well as lack of a well defined sentinel lymph node mapping algorithm considering region (para-aortic and pelvic), side (right and left) of the lymphatic pathway, and ultrastaging protocol on negative sentinel lymph node biopsy. The negative predictive value helps customize treatment choices, but an expected positive case rate serves as an internal control.
- ▶ Sentinel lymph node biopsy is a standard procedure in the staging of many early stage solid tumors. The concept has evolved from very superficial cancer to less superficial, but still with essentially local spread.³⁻⁵ Ovarian cancer is a different tumor whose origin from the mesothelium favors mainly spread to the peritoneal surface. Can injection of tracer in a thin layer of the peritoneum instead of a dense tissue as in the cervix, vulva, or breast affect

the detection rate? The reported 92% detection rate in this meta-analysis may appear an over-estimation due to identifying fatty tissue rather than lymphatic pathways. Previous excision of the tumor is not a contraindication for sentinel lymph node restaging in vulvar and breast cancer after conization for cervical cancer. What about removal of the ovarian mass prior to dye injection? There are data showing a sensible reduction in detection rate during restaging procedures, if the infundibolo-pelvic ligament has been previously ligated.⁶ If this is the case, is it advisable to inject and dissect the retroperitoneum before having a histological diagnosis of cancer? Should we acknowledge the possibility of spillage in upcoming trials? Finally, how do micrometastasis and isolated tumor cells in ovarian cancer prognosticate compared with other gynecological cancers?

- ▶ Omic sciences, AI driven algorithms, and advanced technologies have unveiled novel domains with the potential to impact the sentinel lymph node concept: liquid biopsy assays may identify minimal residual disease, either in tandem with or surpassing sentinel lymph node biopsy information; tumor molecular profiling may provide useful prognostic factors regardless surgical staging; and antibody-dye conjugates could enhance the accuracy of positive node detection. Is it too late to propose a standard sentinel lymph node biopsy approach for early stage ovarian cancer?

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