



<sup>1</sup>Gynecologic Oncology, Dipartimento per le Scienze della salute della donna e del bambino, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy  
<sup>2</sup>Università Cattolica del Sacro Cuore, Rome, Italy

#### Correspondence to

Dr Anna Fagotti, Agostino Gemelli IRCCS, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Lazio, Italy; [anna.fagotti@policlinicogemelli.it](mailto:anna.fagotti@policlinicogemelli.it)

Received 15 August 2023  
 Accepted 17 August 2023  
 Published Online First  
 4 September 2023



► <http://dx.doi.org/10.1136/ijgc-2023-004572>



© IGCS and ESGO 2023. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Fagotti A, Nero C. *Int J Gynecol Cancer* 2023;**33**:1502–1503.

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

Anna Fagotti <sup>1,2</sup>, Camilla Nero<sup>1,2</sup>

In this month's Lead Article, Agustí 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.<sup>1</sup> 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,<sup>2</sup> 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.<sup>3–5</sup> 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.<sup>6</sup> 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?

**Correction notice** This article has been corrected since it was first published. A typographical error in the first sentence has been corrected.

**Twitter** Anna Fagotti @annafagottim

**Contributors** Both authors contributed to the writing and revising of this manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial, or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; internally peer reviewed.

## ORCID ID

Anna Fagotti <http://orcid.org/0000-0001-5579-335X>

## REFERENCES

- 1 Agusti N, Viveros-Carreño D, Grillo-Ardila C, *et al.* Sentinel lymph node detection in early-stage ovarian cancer: a systematic review and meta-analysis. *Int J Gynecol Cancer* 2023;33:1493–501.
- 2 Maggioni A, Benedetti Panici P, Dell'Anna T, *et al.* Randomized study of systematic lymphadenectomy in patients with epithelial ovarian cancer macroscopically confined to the pelvis. *Br J Cancer* 2006;95:699–704.
- 3 Veronesi U, Viale G, Paganelli G, *et al.* Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. *Ann Surg* 2010;251:595–600.
- 4 Wong SL, Faries MB, Kennedy EB, *et al.* Sentinel lymph node biopsy and management of regional lymph nodes in melanoma: American Society of Clinical Oncology and Society of Surgical Oncology clinical practice guideline update. *Ann Surg Oncol* 2018;25:356–77.
- 5 Chow S, Karam A. Role of sentinel lymph node biopsy for gynecologic cancers. *Curr Opin Obstet Gynecol* 2022;34:15–9.
- 6 Uccella S, Nero C, Vizza E, *et al.* Sentinel-node biopsy in early-stage ovarian cancer: preliminary results of a prospective Multicentre study (SELLY). *Am J Obstet Gynecol* 2019;221:324.