



# Isolated nodal recurrence in endometrial cancer: not so common and very salvageable

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Received 27 June 2023

Accepted 28 June 2023

Published Online First

17 July 2023

Sentinel lymph node mapping is currently considered standard in many centers when performing staging for early endometrial cancer.<sup>1</sup> One major concern when performing sentinel lymph node mapping alone is the risk of isolated recurrence to the lymph nodes, particularly in the setting of no initial attempt at complete lymphadenectomy. Isolated lymph node recurrence is rare in patients with endometrial cancer, and the predictive factors and treatment options that improve overall survival in patients with such recurrence are not well established.<sup>2,3</sup> Of the few studies published thus far on isolated lymph node recurrence in endometrial cancer, the impact of the location of recurrence on survival has not been investigated.<sup>2,3</sup>

In this month's Lead Article, Capasso and colleagues aimed to evaluate the clinicopathological features and outcomes associated with isolated lymph node recurrence in endometrial cancer patients.<sup>4</sup> The primary outcome of the study was cause specific survival stratified by location of recurrence and treatment type. The investigators included 4216 surgically staged endometrial cancer patients at the Mayo Clinic. Of these, 66 patients (1.6%) were diagnosed with isolated lymph node recurrence and stratified by location of recurrence: pelvic, para-aortic, distant, and multiple sites. For all patients with isolated lymph node recurrence, the median cause specific survival was 48 months and did not vary based on location. Although no significant difference was found among location of isolated recurrence, the authors were able to draw conclusions on other factors that impacted survival in this population.

This study demonstrates that low grade histology and absence of lymphovascular space invasion in primary tumors is predictive of improved prognosis in patients with isolated lymph node recurrence. This conclusion is not surprising given that lymphovascular space invasion and/or high grade histology corresponds to more aggressive behavior and worsened prognosis in patients with endometrial cancer.<sup>5,6</sup> It is interesting, however, that other established features of poor prognosis were not significant prognostic factors in patients with isolated lymph node recurrence. A better understanding of why these risk factors (tumor size, International Federation of Gynecology and Obstetrics (FIGO) stage, histology, and

myometrial invasion) are not significantly different should be assessed in future studies.

Another conclusion from this study is that surgical management, with or without additional treatment, is associated with improved survival in patients with isolated lymphatic recurrence. Careful consideration should be made when applying this finding to clinical practice. It is likely that healthier patients with a higher likelihood of radical resection were selected for surgery, whereas patients with poor performance and unfeasible resections did not undergo surgery. The fact that 47% of patients with isolated lymphatic recurrence in the para-aortic region were long term survivors might indicate that such patients may be very salvageable with either radiation alone or surgery followed by radiotherapy. These findings could be challenged because they do not provide sufficient data to determine if surgery would, in fact, provide the same benefit to patients with isolated nodal recurrence in extra-abdominal sites such as the axilla, supraclavicular region, or the groin. Would patients with disease at these sites also benefit from surgical resection? It should also be considered that only 18 patients with isolated lymph node recurrence underwent resection, with or without other treatments, making further assessments within this group challenging. Although this study is limited, it does concur with other studies in the literature that state that surgery, with or without other therapies, is the preferred option for endometrial cancer patients diagnosed with isolated lymph node recurrence.<sup>2,3</sup>

Another point to consider when evaluating oncologic outcomes is the duration of inclusion of the study (1984–2017). Over the course of this time period there have been major changes to the indications for resection of recurrent disease, mode of therapy used in the postoperative period, imaging technology that surely impacted patient selection for surgery, use of novel and targeted therapies, and numerous other factors that might have impacted the outcomes of the study.

The authors of this study should be commended for such an extensive analysis to address an important question pertaining to isolated recurrences. However, many unanswered questions remain about the criteria for patient selection for surgery versus radiotherapy versus systemic treatment. Similarly, we await data



► <http://dx.doi.org/10.1136/ijgc-2023-004435>



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**To cite:** Yates EM, Ramirez PT. *Int J Gynecol Cancer* 2023;**33**:1179–1180.

## Editorial

from studies such as ALICE (Sentinel Node Mapping in High Risk Endometrial Cancer) and the ENDO-3 (Sentinel Node Biopsy in Endometrial Cancer) trial to determine the rates of isolated nodal recurrence in the setting of sentinel lymph node alone or in the setting of no lymph node staging at all, respectively.<sup>7,8</sup>

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**Contributors** Both authors critically reviewed the lead article and composed the editorial.

**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** Commissioned; internally peer reviewed.

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