Editorial

Knowing when to hold and when to fold: sentinel lymph node biopsy in endometrial intraepithelial neoplasia

Anousheh Shafa, Andrea Mariani [ID], Gretchen Glaser [ID]

Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minnesota, USA

Correspondence to
Dr Gretchen Glaser, Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minnesota 55905, USA; glaser.gretchen@mayo.edu

► http://dx.doi.org/10.1136/ijgc-2022-003521

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To perform or not perform a sentinel lymph node (SLN) biopsy in endometrial intraepithelial neoplasia—that is the question. While most patients with this pre-operative diagnosis and a post-operative histology of endometrial cancer have early-stage, low-grade disease, approximately 10% require lymph node assessment to guide adjuvant treatment.[1 2] As there are currently no widely accepted pre-operative guidelines for SLN assessment in endometrial intraepithelial neoplasia, the work of Abt et al, is particularly important.[3]

The Mayo criteria identify a low-risk group of patients with endometrial cancer (grade 1 or 2, tumor diameter ≤2 cm, myoinvasion ≤50%, and no intra-operative evidence of macroscopic disease) who can be treated with hysterectomy alone. All others are considered 'at-risk' by Mayo criteria and should ideally undergo lymph node assessment.[4] The Mayo criteria were developed when systematic pelvic ±para-aortic lymphadenectomy was performed for lymph node assessment, a procedure that has a 23% attributable risk of lower extremity lymphedema after surgery.[5] Replacing this practice with SLN biopsy has significantly reduced treatment-related morbidity and does not increase the risk of lower extremity lymphedema over hysterectomy alone.[6]

The authors of this month's lead article performed a retrospective cohort study at a single institution, reviewing 378 patients with a planned hysterectomy for endometrial intraepithelial neoplasia. In their population, 27% had a final pathologic diagnosis of endometrial cancer, of whom 31% were considered 'at-risk' for lymph node metastasis by Mayo criteria. When looking for possible pre-operative markers of concurrent endometrial cancer in patients with endometrial intraepithelial neoplasia, the authors noted that patients with endometrial thickness ≥15 mm (measured at ultrasound) were 1.8 times more likely to have endometrial cancer than those with endometrial thickness <15 mm, and 2.5 times more likely to meet Mayo criteria for lymph node assessment.

When considering whether to perform SLN biopsy at the time of hysterectomy for endometrial intraepithelial neoplasia, it is important to consider what is at stake. When omitting lymph node assessment in patients 'at risk', there is the potential morbidity of repeat surgery with lymphadenectomy and/or adjuvant radiotherapy.[1 2] Therefore, as we attempt to identify patients who will not benefit from surgical staging, false-negative results must be minimized.

As summarized in table 1, the authors of the lead article suggest performing SLN biopsy in patients with ≥15 mm endometrial thickness (32% of the overall population). This approach offers a 17% probability of finding patients 'at risk'. Considering the overall population of 310 patients with available information, we would potentially miss only eight patients (2.6%) who should have lymph node assessment according to Mayo criteria. These data demonstrate a low false-negative rate. In addition, we should consider that only 2–8% of the total endometrial intraepithelial neoplasia population will have high-risk characteristics (such as deep myoinvasion or high grade) on the hysterectomy specimen.[1 2] Therefore, any effort to identify this higher-risk population of patients who may benefit from surgical staging is meritorious.

Table 1 Probability of finding patients "at-risk" for lymph node metastasis by Mayo criteria

	Endometrial thickness (mm)	Fraction (%) of patients from the total population	Number (%) of patients with endometrial cancer meeting Mayo criteria
Abt et al[3]	≥15 (n=100)	32%	17 (17%)
	<15 (n=210)	68%	8 (4%)
	≥20 (n=43)	14%	9 (21%)
	<20 (n=267)	86%	16 (6%)
Vetter et al[1]	≥20 (n=30)	18%	10 (33%)
	<20 (n=139)	82%	13 (9%)

n, total number of patients with endometrial intraepithelial neoplasia in pre-operative biopsy.

Ideally, the addition of pathologic or molecular characteristics of the pre-operative biopsy[2 7 8] can further refine this approach and create an even more comprehensive algorithm. Moreover, in some centers (like the Mayo Clinic), an intra-operative frozen section of the uterus, obtained after mapping and identification of the SLN, can greatly contribute to the decision of whether to remove SLNs at the time of hysterectomy.

We commend the authors for their contribution to creating a pre-operative risk stratification algorithm for endometrial intraepithelial neoplasia. This adds valuable knowledge for gynecologic oncologists, as well as important triage information for gynecologists when gynecologic oncology care is not available due to geographic constraints. By further refining the pre-operative algorithm we may truly be able to know when to hold and when to fold.

Twitter Anousheh Shafa @anousheh.shafa

Contributors All the authors contributed substantially to the paper and approved the final version.

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.

ORCID iDs
Andrea Mariani http://orcid.org/0000-0001-8059-1602
Gretchen Glaser http://orcid.org/0000-0001-9413-316X

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