SUPPLEMENTAL MATERIAL

Table S1. Lymph node dissection other than sentinel lymph node.

Characteristic	Node negative cohort N=452	SLN-ITC cohort N=42	P†
Pelvic LND			0.99
No	379 (83.8)	35 (83.3)	
Yes	73 (16.2)	7 (16.7)	
Positive pelvic LND			-
No	452 (100.0)	42 (100.0)	
Yes	0	0	
Paraaortic LND			0.30
No	449 (99.3)	41 (97.6)	
Yes	3 (0.7)	1 (2.4)	
Positive paraaortic LND			-
No	452 (100.0)	42 (100.0)	
Yes	0	0	

Abbreviations: ITC, isolated tumor cell; LND, lymphadenectomy; SLN, sentinel lymph node.
†Fisher's exact test P value.

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Table S2. Patients with recurrence*.

Patient	SLN node status	Age at surgery (years)	FIGO grade	LVSI	MI (%)	Peritoneal cytology	Largest tumor diameter (mm)	Number of SLNs removed	LND pathology (# nodes removed: P, PA)	Recurrence	Time to first recurrence (months)	Treatment of first recurrence	Vital status
1	Node Negative	73	1	No	0	Not sampled	28	7	No LND	Peritoneal	18.1	CT	Dead
2	ITC	83	1	No	38	Negative	43	3	No LND	Hematogenous	23.1	Unknown	Dead
3	Node Negative	64	1	No	17	Negative	60	3	No LND	Lymphatic (pelvic and paraaortic)	23.2	EBRT	Alive
4	Node Negative	84	1	No	0	Negative	1	3	Negative (17)	Other (vulvar)	32.3	Surgery	Alive
5	Node Negative	61	1	No	10	Positive	26	2	Negative (10)	Hematogenous and peritoneal	44.9	CT	Alive
6	Node Negative	57	1	No	47	Negative	55	5	No LND	Hematogenous and lymphatic (pelvic and paraaortic)	57.7	CT	Dead
7	Node Negative	62	1	Yes	37	Not sampled	34	5	No LND	Hematogenous	43.9	Letrozole	Alive
8	ITC	58	2	No	20	Negative	48	4	No LND	Lymphatic (pelvic)	11.7	None	Alive

9	ITC	58	2	No	10	Not sampled	45	3	Negative (15, 21)	Peritoneal and vaginal	6.0	CT	Alive
10	Node Negative	79	2	No	35	Negative	29	3	No LND	Hematogenous and vaginal	14.2	CT+EBRT+ pembrolizumab	Dead
11	Node Negative	65	2	No	0	Negative	72	3	No LND	Lymphatic (pelvic) and peritoneal	17.1	CT	Alive
12	Node Negative	57	2	No	27	Negative	11	2	No LND	Hematogenous	51.3	CT	Alive
13	Node Negative	61	2	No	45	Negative	36	4	No LND	Lymphatic (pelvic)	57.2	Surgery+CT+EBRT	Alive
14	Node Negative	79	2	No	8	Negative	18	4	No LND	Peritoneal and vaginal	57.3	None	Dead
15	ITC	60	2	Yes	44	Not sampled	/	2	No LND	Lymphatic (pelvic and groin)	4.3	CT+EBRT+VB	Alive
16	Node Negative	66	1	No	17	Negative	70	4	No LND	Vaginal	21.1	EBRT	Alive
17	Node Negative	61	1	No	12	Negative	62	4	No LND	Vaginal	25.5	Surgery	Alive
18	ITC	65	1	Yes	26	Negative	37	2	No LND	Vaginal	14.7	CT+EBRT+VB	Alive

19	Node Negative	48	2	No	48	Negative	78	2	No LND	Vaginal	7.8	Surgery+CT	Alive
20	Node Negative	59	2	No	0	Negative	35	2	No LND	Vaginal	30.6	EBRT+VB	Alive
21	Node Negative	58	2	Yes	23	Not sampled	41	3	No LND	Vaginal	26.1	EBRT+VB	Alive

Abbreviations: BMI, body mass index; CT, chemotherapy; EBRT, external beam radiation therapy; FIGO, International Federation of Gynecology and Obstetrics; LND, lymphadenectomy; LVSI, lymphovascular space invasion; MI, myometrial invasion; P, pelvic; PA, paraaortic; SLN, sentinel lymph node; VB, vaginal brachytherapy; ITC, isolated tumor cells.

*All patients listed were FIGO stage IA and had bilateral SLN removal.

Table S3. Distribution of non-vaginal recurrences among the overall low-risk population (stage IA, endometrioid histology, grade 1 or 2) according to the main histopathological features.

SLN node status	Grade	LVSI	N	N of patients with non-vaginal recurrence (%)	Years to recurrence Median (range)
Node negative	1	No	342	5 (1.5)	2.7 (1.5-4.8)
Node negative	1	Yes	5	1 (20.0)	3.7 (-)
Node negative	2	No	103	5 (4.9)	4.3 (1.2-4.8)
Node negative	2	Yes	2	0 (0)	-
ITC	1	No	24	1 (4.2)	1.9 (-)
ITC	1	Yes	5	0 (0)	-
ITC	2	No	11	2 (18.2)	0.7 (0.5-1.0)
ITC	2	Yes	2	1 (50.0)	0.4 (-)

Abbreviations: ITC, isolated tumor cell; LVSI, lymphovascular space invasion; SLN, sentinel lymph node.

Appendix

Surgical management

All patients underwent surgical staging for endometrial cancer (including hysterectomy, bilateral salpingo-oophorectomy, and SLN biopsy) at one of the participating centers. Sentinel lymph node mapping was performed following National Comprehensive Cancer Network (NCCN) SLN mapping guidelines (1). SLNs were ultrastaged using the Memorial Sloan-Kettering Cancer Center approach (2) or a modification of this protocol based on each institution's anatomic pathology protocols.

Data collection

Each participating center collected data regarding demographic, clinical, tumor, treatment, and outcome characteristics. Demographic, clinical, and pathology data were obtained by reviewing the electronic medical record and entered in a secure REDCap database, as previously described (3). Location of the recurrence was classified as: vaginal, peritoneal, hematogenous, lymphatic (pelvic, paraaortic, other distant lymphatic – inguinal, mediastinal, supraclavicular). Non-vaginal recurrence was defined as recurrence localized to the lymph nodes or peritoneum or was distant through hematogenous spread, with or without concomitant vaginal recurrence.

Statistical methods

Clinicopathologic characteristics and variables of lymph node dissection other than SLN were compared between two cohorts (SLN-ITC patients versus node-negative patients) utilizing chi-square or Fisher's exact tests for categorical variables and the two-sample t-test for continuous variables. The Kaplan-Meier method was used to estimate overall, recurrence-free, and non-vaginal recurrence-free survival by cohort, SLN-ITC and node-negative patients, restricting follow-up to the first 5 years after surgery. These were repeated excluding patients with lymphovascular space invasion. Time-to-event was calculated from the date of surgery to the date of death or last follow-up for overall survival

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and from the date of surgery to the date of recurrence or last relevant clinical follow-up for recurrence-free survival.

Univariate and multivariable Cox proportional hazards regression models were fit to evaluate the association between clinicopathologic characteristics with death and recurrence (any and non-vaginal). Associations were summarized with a hazard ratio (HR) and 95% confidence interval (CI). All calculated P values were two-sided, and $P<0.05$ was considered statistically significant. Statistical analyses were performed using the SAS 9.4 (SAS Institute, Inc).

References

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3. Ghoniem K, Larish AM, Dinoi G, Zhou XC, Alhilli M, Wallace S, et al. Oncologic outcomes of endometrial cancer in patients with low-volume metastasis in the sentinel lymph nodes: An international multi-institutional study. Gynecol Oncol. 2021;162(3):590-8.

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