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The prognostic evaluation of lymph-vascular space invasion to patients with endometrioid cancer and non-endometrioid cancer

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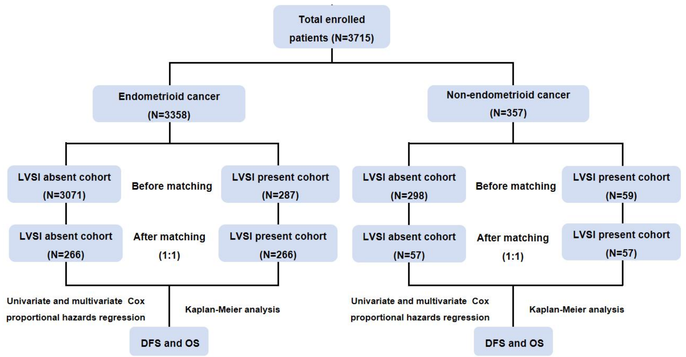
Background

- The impact of lymph-vascular space invasion (LVSI) on the prognosis of endometrial cancer (EC) patients remains controversial and lacks support from large sample size studies. Very few have examined whether LVSI is related to prognosis of non-endometrioid cancer patients.
- We conduct a multicenter cohort study to compare the impact of LVSI on the prognosis between patients with endometrioid and non-endometrioid cancer.

Methods

- This is a retrospective cohort study from six hospitals in China.
- Key inclusion criteria:
  1) underwent surgery as initial treatment
  2) without other malignancies
  3) complete follow-up outcomes
- Statistical analysis:
  1) Propensity score matching (PSM) algorithm
  2) Univariate and multivariate Cox proportional hazards regression analysis
  3) Kaplan-Meier analysis



Results

- This study included 3358 endometrioid and 357 non-endometrioid cancer patients. The LVSI positive rate was 8.55% (287/3358) in the endometrioid cancer patients and 16.53% (59/357) in the non-endometrioid cancer patients.
- In a multivariate Cox proportional hazards regression analysis, LVSI was an independent risk factor of DFS (hazard ratio [HR], 2.62 [95% CI, 1.35-5.10]; P=0.005) and not OS (HR, 1.24 [95% CI, 0.49-3.13]; P=0.66) for endometrioid cancer patients. LVSI was not a prognostic factor of neither DFS (HR, 1.28 [95% CI, 0.58-2.81]; P=0.54) or OS (HR, 1.33 [95% CI, 0.55-3.13]; P=0.52) for non-endometrioid cancer patients.

Conclusion

- LVSI is an adverse prognostic factor for patients with endometrioid cancer, but not for patients with non-endometrioid cancer. For patients with positive LVSI, further postoperative treatment should be considered for endometrioid cancer patients, while the necessity of adjuvant therapy needs to be carefully evaluated for non-endometrioid cancer patients.

Table 1. Characteristics of patients in the before and after PSM cohorts

Characteristic	All patients				Endometrioid cancer population				Non-endometrioid cancer population			
	Total (n=3715)	LVSI absent (n=3369)	LVSI present (n=346)	*P*	Total (n=3358)	LVSI absent (n=3071)	LVSI present (n=287)	*P*	Total (n=357)	LVSI absent (n=298)	LVSI present (n=59)	*P*
Age (years)				0.17				0.77				0.41
< 60	2767 (74.5)	2520 (74.8)	247 (71.4)		2574 (76.7)	2356 (76.7)	218 (76.0)		193 (54.1)	164 (55.0)	29 (49.2)	
≥ 60	948 (25.5)	849 (25.2)	99 (28.6)		784 (23.3)	715 (23.3)	69 (24.0)		164 (45.9)	134 (45.0)	30 (50.8)	
Menopausal status				0.29				0.77				0.36
No	1574 (42.4)	1441 (42.8)	133 (38.4)		1482 (44.1)	1361 (44.3)	121 (42.2)		92 (25.8)	80 (26.8)	12 (20.3)	
Yes	2058 (55.4)	1854 (55.0)	204 (59.0)		1804 (53.7)	1644 (53.5)	160 (55.7)		254 (71.1)	210 (70.5)	44 (76.8)	
Unknown	83 (2.2)	74 (2.2)	9 (2.6)		72 (2.1)	66 (2.1)	6 (2.1)		11 (3.1)	8 (2.7)	3 (5.1)	
BMI (kg/m²)				0.23				0.19				0.27
< 24	873 (23.5)	786 (23.3)	87 (25.1)		797 (23.7)	727 (23.7)	70 (24.4)		76 (21.3)	59 (19.8)	17 (28.8)	
≥ 24	1209 (32.5)	1087 (32.3)	122 (35.3)		1124 (33.5)	1016 (33.1)	108 (37.6)		85 (23.8)	71 (23.8)	14 (23.7)	
Unknown	1633 (44.0)	1496 (44.4)	137 (39.6)		1437 (42.8)	1328 (43.2)	109 (38.0)		196 (54.9)	168 (56.4)	28 (47.5)	
Baseline CA-125 (U/ml)				<0.001				<0.001				0.25
≤ 35	2125 (57.2)	1959 (58.1)	166 (48.0)		1940 (57.8)	1802 (58.7)	138 (48.1)		185 (51.8)	157 (52.7)	28 (47.5)	
> 35	708 (19.1)	579 (17.2)	129 (37.3)		639 (19.0)	526 (17.1)	113 (39.4)		69 (19.3)	53 (17.8)	16 (27.1)	
Unknown	882 (23.7)	831 (24.7)	51 (14.7)		779 (23.2)	743 (24.2)	36 (12.5)		103 (28.9)	88 (29.5)	15 (25.4)	
Surgical route				0.04				0.10				0.69
Laparotomy	2051 (55.2)	1842 (54.7)	209 (60.4)		1811 (53.9)	1643 (53.5)	168 (58.5)		240 (67.2)	199 (66.8)	41 (69.5)	
Laparoscopy	1664 (44.8)	1527 (45.3)	137 (39.6)		1547 (46.1)	1428 (46.5)	119 (41.5)		117 (32.8)	99 (33.2)	18 (30.5)	
Surgery scope				<0.001				<0.001				0.21
TH	91 (2.4)	88 (2.6)	3 (0.9)		87 (2.6)	84 (2.7)	3 (1.0)		4 (1.1)	4 (1.3)	0 (0.0)	
TH + BSO	804 (21.6)	772 (22.9)	32 (9.2)		755 (22.5)	727 (23.7)	28 (9.8)		49 (13.7)	45 (15.1)	4 (6.8)	
TH + BSO + surgical staging	2820 (75.9)	2509 (74.5)	311 (89.9)		2516 (74.9)	2260 (73.6)	256 (89.2)		304 (85.2)	249 (83.6)	55 (93.2)	
Peritoneal cytology				0.90				0.88				0.25
Negative	1488 (40.1)	1346 (40.0)	142 (41.0)		1294 (38.5)	1180 (38.4)	114 (39.7)		194 (54.3)	166 (55.7)	28 (47.5)	
Positive	102 (2.7)	92 (2.7)	10 (2.9)		92 (2.7)	85 (2.8)	7 (2.4)		10 (2.8)	7 (2.3)	3 (5.1)	
Unknown	2125 (57.2)	1931 (57.3)	194 (56.1)		1972 (58.7)	1806 (58.8)	166 (57.8)		153 (42.9)	125 (41.9)	28 (47.5)	
Grade				<0.001				<0.001				0.05
G1+G2	3033 (81.6)	2830 (84.0)	203 (58.7)		2858 (85.1)	2677 (87.2)	181 (63.1)		175 (49.0)	153 (51.3)	22 (37.3)	
G3	682 (18.4)	539 (16.0)	143 (41.3)		500 (14.9)	394 (12.8)	106 (36.9)		182 (51.0)	145 (48.7)	37 (62.7)	
Myometrial invasion depth				<0.001				<0.001				0.006
None	414 (11.1)	411 (12.2)	3 (0.9)		375 (11.2)	374 (12.2)	1 (0.3)		39 (10.9)	37 (12.4)	2 (3.4)	
< 1/2	2524 (67.9)	2358 (70.0)	166 (48.0)		2331 (69.4)	2192 (71.4)	139 (48.4)		193 (54.1)	166 (55.7)	27 (45.8)	
≥ 1/2	665 (17.9)	496 (14.7)	169 (48.8)		559 (16.6)	418 (13.6)	141 (49.1)		106 (29.7)	78 (26.2)	28 (47.5)	
Unknown	112 (3.0)	104 (3.1)	8 (2.3)		93 (2.8)	87 (2.8)	6 (2.1)		19 (5.3)	17 (5.7)	2 (3.4)	
FIGO (2009) stage				<0.001				<0.001				<0.001
I	3044 (81.9)	2883 (85.6)	161 (46.5)		2807 (83.6)	2663 (86.7)	144 (50.2)		237 (66.4)	220 (73.8)	17 (28.8)	
II	268 (7.2)	231 (6.9)	37 (10.7)		232 (6.9)	203 (6.6)	29 (10.1)		36 (10.1)	28 (9.4)	8 (13.6)	
III	356 (9.6)	229 (6.8)	127 (36.7)		286 (8.5)	190 (6.2)	96 (33.4)		70 (19.6)	39 (13.1)	31 (52.5)	
IV	47 (1.3)	26 (0.8)	21 (6.1)		33 (1.0)	15 (0.5)	18 (6.3)		14 (3.9)	11 (3.7)	3 (5.1)	
Adjuvant therapy				<0.001				<0.001				<0.001
None	2309 (62.2)	2262 (67.1)	47 (13.6)		2196 (65.4)	2157 (70.2)	39 (13.6)		113 (31.7)	105 (35.2)	8 (13.6)	
Chemotherapy	818 (22.0)	669 (19.9)	149 (43.1)		671 (20.0)	545 (17.7)	126 (43.9)		147 (41.2)	124 (41.6)	23 (39.0)	
Radiotherapy	189 (5.1)	169 (5.0)	20 (5.8)		178 (5.3)	161 (5.2)	17 (5.9)		11 (3.1)	8 (2.7)	3 (5.1)	
Chemotherapy + radiotherapy	399 (10.7)	269 (8.0)	130 (37.6)		313 (9.3)	208 (6.8)	105 (36.6)		86 (24.1)	61 (20.5)	25 (42.4)	

Table 2. Multivariate Cox proportional hazards regression analysis for DFS and OS in the after PSM cohort

Characteristic	Endometrioid cancer population				Non-endometrioid cancer population			
	DFS		OS		DFS		OS	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
LVSI								
Absent	Reference		-		-		-	
Present	2.62 (1.35-5.10)	0.005	-		-		-	
Age (years)								
< 60	Reference		-		Reference		Reference	
≥ 60	2.18 (1.13-4.21)	0.02	-		5.91 (2.17-16.07)	0.001	10.51 (2.91-37.97)	<0.001
Grade								
G1+G2	Reference		-		-		-	
G3	3.16 (1.68-5.98)	<0.001	-		-		-	
FIGO (2009) stage								
I	Reference		Reference		Reference		Reference	
II	1.61 (0.57-4.60)	0.37	-		4.82 (1.18-19.72)	0.03	3.94 (0.90-17.16)	0.07
III	3.64 (1.79-7.39)	<0.001	7.81 (2.20-27.69)	0.001	3.61 (1.02-12.81)	0.05	2.87 (0.78-10.60)	0.12
IV	2.53 (0.57-11.29)	0.22	18.50 (3.72-92.09)	<0.001	19.97 (3.67-108.75)	0.001	22.32 (4.13-120.62)	<0.001

Abbreviations: PSM, propensity score matching; LVSI, lymph-vascular space invasion; BMI, body mass index; CA-125, cancer antigen 125; FIGO, International Federation of Gynecology and Obstetrics; TH, total hysterectomy; BSO, bilateral salpingo-oophorectomy; G, histopathologic grades; DFS, disease-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interva.
Empty cells: no statistical difference.

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Conflict of interests: None

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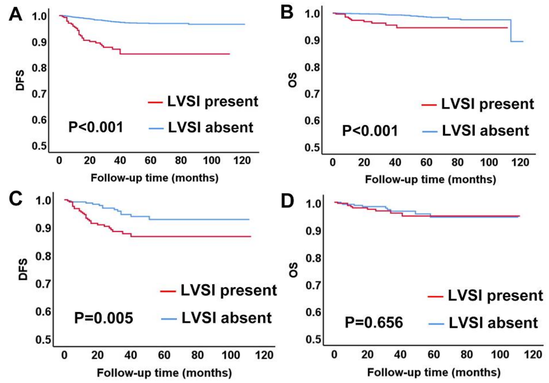
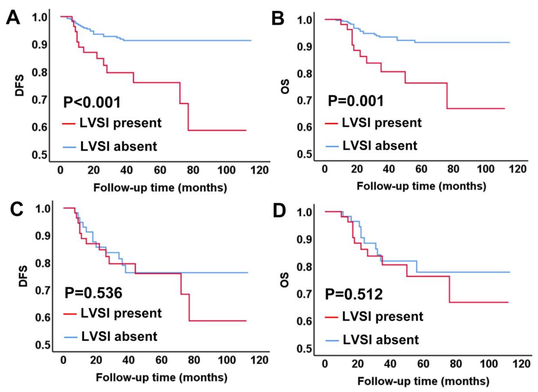
Kaplan-Meier curves for the before (A/B) and after (C/D) PSM cohorts

For patients with endometrioid cancer, there was statistical difference of disease-free survival (DFS, C), but not the overall survival (OS, D) between LVSI present and absent cohorts after PSM.



While, for patients with non-endometrioid cancer, there was no statistical difference in neither DFS (C) or OS (D) after PSM.



Survival of patients with endometrioid cancer

	LVSI absent group	LVSI present group
5-year DFS	97.0%	85.2%
5-year OS	98.5%	94.5%

Survival of patients with non-endometrioid cancer

	LVSI absent group	LVSI present group
5-year DFS	91.3%	76.0%
5-year OS	91.4%	76.3%

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