RESEARCH ARTICLE

Editorial Process: Submission:25/12/2025 Acceptance:17/08/2026 Published:21/08/2026

Prognostic Value of Lymphovascular Space Invasion and Its Quantification in Endometrial Carcinoma in Northern Thailand

Tip Pongsuvareeyakul[1], Panruethai Wongkampan[1], Phitchayut Phinyo[2], Noraworn Jirattikanwong[2], Chalong Cheewakriangkrai[3], Kornkanok Sukpan[1], Jongkolnee Settakorn[1], Sumalee Siriaunkgul[1], Surapan Khunamornpong[1]*

Abstract

Objective: To evaluate the prognostic performance of lymphovascular space invasion (LVSI) quantification in patients with endometrial carcinoma (EC). **Methods:** Clinical and pathological data from EC patients who underwent primary surgical treatment between January 2008 and December 2020 were analyzed. Five-year progression-free survival (PFS) and overall survival (OS) were compared across LVSI categories (absent, focal, substantial) using previously proposed thresholds for substantial LVSI (≥3, ≥4, or ≥5 involved spaces). **Results:** A total of 843 patients were included (mean follow-up, 9.5 years). All three thresholds (3, 4, or 5 spaces) yielded significant differences in PFS and OS across LVSI categories (absent, focal, and substantial; $p < 0.001$). After adjustment for established clinicopathologic prognostic factors, substantial LVSI remained independently associated with worse PFS and OS compared with absent LVSI (PFS: $p = 0.005$-0.007; OS: $p = 0.002$-0.006). Focal LVSI, defined as <4 or <5 spaces, showed a trend toward lower adjusted PFS compared with absent LVSI, although the difference did not reach statistical significance ($p = 0.052$–0.059). For OS, focal LVSI showed worse adjusted outcomes than absent LVSI when using the <5-space definition ($p = 0.024$). No significant adjusted differences in PFS or OS were observed between focal and substantial LVSI. **Conclusion:** Substantial LVSI (at least 3 involved spaces) is strongly associated with poorer prognosis in EC. Additionally, focal LVSI may be linked to decreased survival. These findings underscore the prognostic value of LVSI quantification and support further investigation into the clinical relevance of focal LVSI.

Keywords: Endometrial carcinoma, Lymphovascular space invasion, Prognostic value, Quantification

Asian Pac J Cancer Prev, **27 (8)**, 3021-3027

Introduction

Endometrial carcinoma (EC) is the sixth most common cancer in female worldwide, with an annual incidence of 32,000 new cases [1]. The management decision for EC patients is based on tumor staging, which comprises multiple risk parameters including histopathological features and/or molecular profiles if available [2]. LVSI was found to be one of the strongest predictors for lymph node metastasis and disease recurrence in EC patients [3-5]. The evaluation of LVSI is based on microscopic examination, without the use of immunohistochemistry, allowing this approach feasible in routine practice, even in a low-resource setting.

When LVSI is present, the number of LVSI is semi-quantitatively categorized as focal and substantial. Substantial LVSI has been defined with some variation in the cut-off values across different guidelines: 3 spaces by the International Collaboration on Cancer Reporting (ICCR) [6], 4 spaces by the National Comprehensive Cancer Network (NCCN) [7], and 5 spaces by World Health Organization (WHO) and Collage of American Pathologists (CAP) [8]. The presence of substantial LVSI has been accepted as an important feature for EC risk stratification by the European Society for Medical Oncology (ESMO), the European Society of Gynaecological Oncology (ESGO), and the European Society of Pathology (ESP) in 2021 [9], and has been included in the recent 2023 FIGO staging system [2]. Focal LVSI has been classified in the same risk category as absent LVSI in management guidelines [2, 9]. However, recent studies have challenged this concept, suggesting that focal LVSI could pose a significantly higher prognostic risk compared to absent LVSI, particularly when other risk

*[1]Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. [2]Center for Clinical Epidemiology and Clinical Statistics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. [3]Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. *For Correspondence: skhunamo@yahoo.com*

factors are properly adjusted [10, 11]. In these studies, the risk difference between focal and substantial LVSI was found to be non-significant.

The aim of this study is to evaluate the prognostic impact of LVSI quantification in EC patients at our institution. This study represents real-world experience in the quantification of LVSI within a single-institution setting.

Materials and Methods

Patient collection

The pathology reports of EC patients who underwent hysterectomy between January 2008 and December 2020 were searched from database of gynecological pathology unit, department of Pathology, Chiang Mai University Hospital. Information on patients' staging and outcomes was obtained from the gynecologic oncology records of Chiang Mai University Hospital and Chiang Mai Cancer Registry. Inclusion criteria were patients who had available pathological report information of hysterectomy specimen and had FIGO staging available in the medical records. Patients who received preoperative neoadjuvant therapy were excluded.

Information collection

In each patient, recorded clinical information (age, stage, and clinical outcomes) and pathological parameters (histology type, size, extent of tumor involvement, LVSI quantity, and lymph node status) were collected. The tumor stage was defined as per 2009 FIGO staging system, or redefined if 1988 FIGO system was initially used. The pathology reporting of EC, including LVSI counting, was performed by a group of gynecologic pathologists. Each pathologist had an at least 1-year training period in gynecologic pathology before practicing. All gross examinations and tissue sampling were either performed or supervised by the attending pathologists, using the protocol of at least 1 section per each cm of tumor size.

The original types of EC based on previous WHO classifications were categorized according to 2023 FIGO system as non-aggressive EC (grade 1 and 2 endometrioid carcinoma) and aggressive EC (grade 3 endometrioid carcinoma, clear cell carcinoma, serous carcinoma, undifferentiated/dedifferentiated carcinoma, mixed carcinoma, and carcinosarcoma). Carcinoma composed of at least 2 histologic types with at least one aggressive EC component was classified as mixed carcinoma.

Statistical analysis

All statistical analyses were performed using STATA version 16 (STATA Corp., Texas, USA). Categorical data were presented as frequencies and percentages, assessed using Chi-square test to examine univariable associations between risk parameters and histology types. Continuous data with normal distributions were described using means and standard deviations (SD) and assessed using Student's t-test. For non-normal distribution, medians and interquartile ranges (IQR) were presented, and Mann-Whitney U test was applied. Kaplan-Meier methods and log-rank test were used to explore associations between risk factors and survival endpoints. A flexible parametric survival regression analysis was conducted to assess the association between risk parameters and both progression-free survival (PFS) and overall survival (OS) to estimate the hazard ratio (HR), 95% confidence interval (CI), and survival probabilities. PFS was defined as the interval from the date of surgery to disease progression. OS was defined as the duration between date of surgery and date of death. Patients who did not experience events by the study's closure or whose final status could not be verified were marked as censored. A p value less than 0.05 was considered statistically significant.

Handling missing data

Multiple imputation with chained equation (MICE) via mi impute chained command was used to generate multiple imputed datasets. The determination of number of imputed datasets followed a two-stage approach aimed at ensuring the replicability of standard error. For generating the imputed datasets, binary logistic regression was chosen for the imputation of binary variables.

Results

A total of 843 EC patients were included during the study period. The mean age was 57 years (range, 23–86 years). Tumor stage was FIGO stage I–II in 65.1% of patients and stage III–IV (advanced) in 34.9%. Histologic types were classified as non-aggressive (grade 1–2 endometrioid) in 513 patients (60.9%), and aggressive in 330 patients (39.1%), comprising 143 grade 3 endometrioid, 41 serous, 19 clear cell, 83 mixed adenocarcinomas, and 44 other types, including 35 carcinosarcomas and 9 undifferentiated or dedifferentiated carcinomas. Pelvic and/or para-aortic lymphadenectomy was performed selectively based on preoperative and intraoperative risk assessment (e.g., tumor grade/histology, tumor size, extrauterine lesions, palpable lymph nodes, and depth of myometrial invasion). Overall, lymphadenectomy was performed in 679 patients (80.5%). Adjuvant treatment was administered to 524 patients (62.2%), comprising 228 patients (56.1%) in the non-aggressive histology group and 296 patients (89.7%) in the aggressive histology group. A comparison of clinical and pathological features between non-aggressive and aggressive histologic types is presented in Table 1.

The median follow-up duration was 9.5 years (95% CI, 9.0–10.0). Among the 843 patients, there were 248 deaths (29.4%). Data on recurrence or disease progression were available for 778 of 843 patients (92.3%). Of these, 139 patients (17.9%) experienced tumor recurrence or progression, with a mean duration of 4.6 years. Table 2 presents the association between risk parameters and progression-free survival (PFS) and overall survival (OS) among all EC patients. Multivariable analysis revealed that PFS was independently correlated with aggressive histology (HR 1.95; 95% CI 1.35–2.82), advanced stage (HR 1.92; 95% CI 1.18–3.12), LVSI (HR 1.78; 95% CI 1.10–2.87), and age (HR 1.02; 95% CI 1.00–1.04). For OS, independent correlations were found with aggressive histology (HR 2.79; 95% CI 1.98-3.92), advanced stage (HR 2.42; 95% CI 1.56-3.75),

Table 1. Comparison of Clinical and Pathological Characteristics between Patients with Non-Aggressive and Aggressive Histologic Types of Endometrial Carcinoma

	Non-aggressive histology (n=513)		Aggressive histology (n=330)		p value
	No.	%	No.	%	
Age (years), mean ± SD	56.2 ± 9.3		59.4 ± 8.9		<0.001
FIGO stage					
I-II	385	75	164	49.7	<0.001
III-IV	128	25	166	50.3	
Tumor size					
<2 cm	90	17.5	28	8.5	<0.001
≥2 cm	423	82.5	302	91.5	
Myometrial invasion					
<50%	310	60.4	122	37	<0.001
≥50%	203	39.6	208	63	
Serosal involvement					
Absent	485	94.5	254	77	<0.001
Present	28	5.5	76	23	
Involvement of lower segment					
Absent	346	67.5	169	51.2	<0.001
Present	167	32.5	161	48.8	
Cervical involvement					
Absent	395	77	197	59.7	<0.001
Present	118	23	133	40.3	
Lymphovascular space invasion					
Absent	313	61	97	29.4	<0.001
Present	200	39	233	70.6	
Lymph node metastasis*					
Absent	337	81.2	177	67	<0.001
Present	78	18.8	87	33	
Adjuvant treatment**					
Absent	222	43.3	30	9.1	<0.001
Present	288	56.1	296	89.7	

* Lymph node metastasis based on 679 patients with lymph node histologic examination including 415 patients with non-aggressive histology and 264 patients with aggressive histology; ** Information was missing from 3 patients with non-aggressive histology and 4 patients with aggressive histology.

cervical involvement (HR 1.55; 95% CI 1.06–2.27), LVSI (HR 1.58; 95% CI 1.06–2.35), age (HR 1.04; 95% CI 1.02–1.06), and adjuvant treatment (HR 0.55; 95% CI 0.36 – 0.85).

Table 3 presents comparisons of 5-year progression risk and 5-year mortality risk in patients stratified by different LVSI cut-off values, with adjustments for age, aggressive histology, advanced stage, tumor size ≥2 cm, myometrial invasion ≥50%, lower segment involvement, cervical involvement, lymph node metastasis, and adjuvant treatment. For 5-year adjusted progression risk, the presence of LVSI was associated with a significantly higher progression risk compared to the absence of LVSI (13.8% vs 9.1%; p = 0.005). As the LVSI cut-off count increased from ≥2 to ≥10 spaces, the 5-year adjusted progression risks for each LVSI group remained within a narrow range of 13.8 – 14.4%. Regarding 5-year adjusted mortality risk, the presence of LVSI was associated with a higher risk compared to the absence of LVSI (19.3% vs 14.7%; p = 0.003). As the LVSI cut-off increased from ≥2 to ≥10 spaces, the 5-year mortality risks remained similar, ranging from 18.1 - 19.8%.

Figures 1 and 2 show Kaplan-Meier plots for PFS and OS of EC patients stratified by LVSI status and cut-off values from 3 to 5 spaces to define substantial LVSI. Patients without LVSI had significantly better PFS and OS than those with any degree of LVSI (log-rank p <0.001 for all; Figure 1A–D, Figure 2A–D). Significant differences in both PFS and OS were observed among 3 groups; (a) absent LVSI, (b) focal LVSI (1-2, 1-3, or 1-4 spaces), and (c) substantial LVSI (≥3, ≥4, or ≥5 spaces) (Figure 1B-D, Figure 2B–D).

Survival outcomes (PFS and OS) stratified by LVSI were further adjusted for independent risk parameters identified in Table 3. After adjustment for age, advanced stage, aggressive histology, cervical involvement, and adjuvant treatment, the adjusted 5-year PFS for patients with LVSI was significantly worse than for those without

Table 3. Comparison of 5-year Progression Risk, 5-Year Mortality Risk, adjusted 5-year Progression Risk and adjusted 5-year Mortality Risk Stratified by Different Cut-off Values of LVSI Count

LVSI count	5-year progression risk (%)	5-year mortality risk (%)	5-year adjusted progression risk* (%)	5-year adjusted mortality risk* (%)
0 (negative)	7.4 (5.2 – 10.6)	10.8 (8.2 – 14.3)	9.1 (6.0 – 12.1)	14.7 (11.3 – 18.0)
≥1	26.8 (22.6 – 31.5)	32.5 (28.2 – 37.1)	13.8 (10.0 – 17.7)*	19.3 (15.6 – 23.0)*
≥2	26.6 (22.2 – 31.6)	32.4 (28.0 – 37.3)	13.0 (9.1 – 16.8)	18.5 (14.8 – 22.3)*
≥3	28.3 (23.7 – 33.6)	34.4 (29.7 – 39.5)	13.9 (9.7 – 18.0)*	19.8 (15.7 – 23.9)*
≥4	29.0 (27.9 – 30.2)	35.3 (30.4 – 40.7)	13.8 (9.5 – 18.0)	19.1 (14.9 – 23.2)*
≥5	29.6 (28.4 – 30.8)	35.2 (30.2 – 40.8)	14.0 (9.6 – 18.4)*	18.4 (14.2 – 22.5)*
≥6	29.2 (28.0 – 30.4)	35.2 (30.1 – 41.0)	13.6 (9.2 – 18.0)	18.1 (14.0 – 22.3)
≥7	30.1 (28.8 – 31.3)	35.7 (30.4 – 41.6)	14.4 (9.7 – 19.0)*	18.9 (14.5 – 23.3)*
≥8	29.5 (28.3 – 30.9)	35.3 (30.0 – 41.3)	14.0 (9.4 – 18.6)	18.6 (14.2 – 23.0)*
≥9	29.4 (28.2 – 30.7)	35.6 (30.1 – 41.6)	13.6 (9.0 – 18.1)	18.4 (14.0 – 22.8)*
≥10	30.7 (29.4 – 32.1)	36.5 (30.9 – 42.7)	14.0 (9.3 – 18.8)	18.3 (13.8 – 22.8)

* Significant difference ($p<0.05$) compared to the LVSI-negative group

Table 2. Analysis for the Association between Risk Parameters and Survival in All Patients at 5 Years

Risk parameters	Progression - free survival* (N=778)				Overall survival* (N=843)			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (years)	1.02 (1.01 – 1.04)	0.009	1.02 (1.00 – 1.04)	0.024	1.05 (1.03 – 1.06)	< 0.001	1.04 (1.02 – 1.06)	<0.001
Advanced stage	4.46 (3.10 – 6.38)	<0.001	1.92 (1.18 – 3.12)	0.008	4.40 (3.24 – 5.98)	<0.001	2.42 (1.56 – 3.75)	<0.001
Aggressive histology	3.82 (2.65 – 5.51)	<0.001	1.95 (1.35 – 2.82)	<0.001	4.16 (3.04 – 5.70)	<0.001	2.79 (1.98 – 3.92)	<0.001
Tumor size ≥2 cm	2.20 (1.15 – 4.19)	0.017	1.33 (0.68 – 2.59)	0.402	1.58 (0.97– 2.57)	0.066	0.83 (0.50 – 1.38)	0.469
Myometrial invasion ≥50%	3.15 (2.16 – 4.60)	<0.001	1.18 (0.77 – 1.79)	0.453	3.36 (2.42 – 4.68)	<0.001	1.46 (0.98 – 2.18)	0.061
Lower segment involvement	2.55 (1.80 – 3.62)	<0.001	1.10 (0.70 – 1.73)	0.667	2.17 (1.62 – 2.91)	<0.001	1.02 (0.69 – 1.50)	0.937
Cervical involvement	2.68 (1.89 – 3.77)	<0.001	1.56 (1.02 – 2.40)	0.04	2.59 (1.93 – 3.46)	<0.001	1.55 (1.06 – 2.27)	0.022
Lymphovascular space invasion	4.04 (2.66 – 6.13)	<0.001	1.78 (1.10 – 2.87)	0.019	3.44 (2.44 – 4.84)	<0.001	1.58 (1.06 – 2.35)	0.024
Lymph node metastasis†	3.19 (2.24 – 4.54)	<0.001	1.17 (0.73 – 1.88)	0.513	3.18 (2.32 – 4.35)	<0.001	1.19 (0.79 – 1.81)	0.403
Adjuvant treatment†	4.66 (2.63 – 8.24)	<0.001	1.54 (0.82 – 2.88)	0.181	2.14 (1.46 – 3.14)	<0.001	0.55 (0.36 – 0.85)	0.007

Abbreviation: HR; Hazard Ratio, CI; Confidence Interval; * Results from flexible parametric survival regression; † Missing data of lymph node metastasis and adjuvant treatment was handled with multiple imputations.

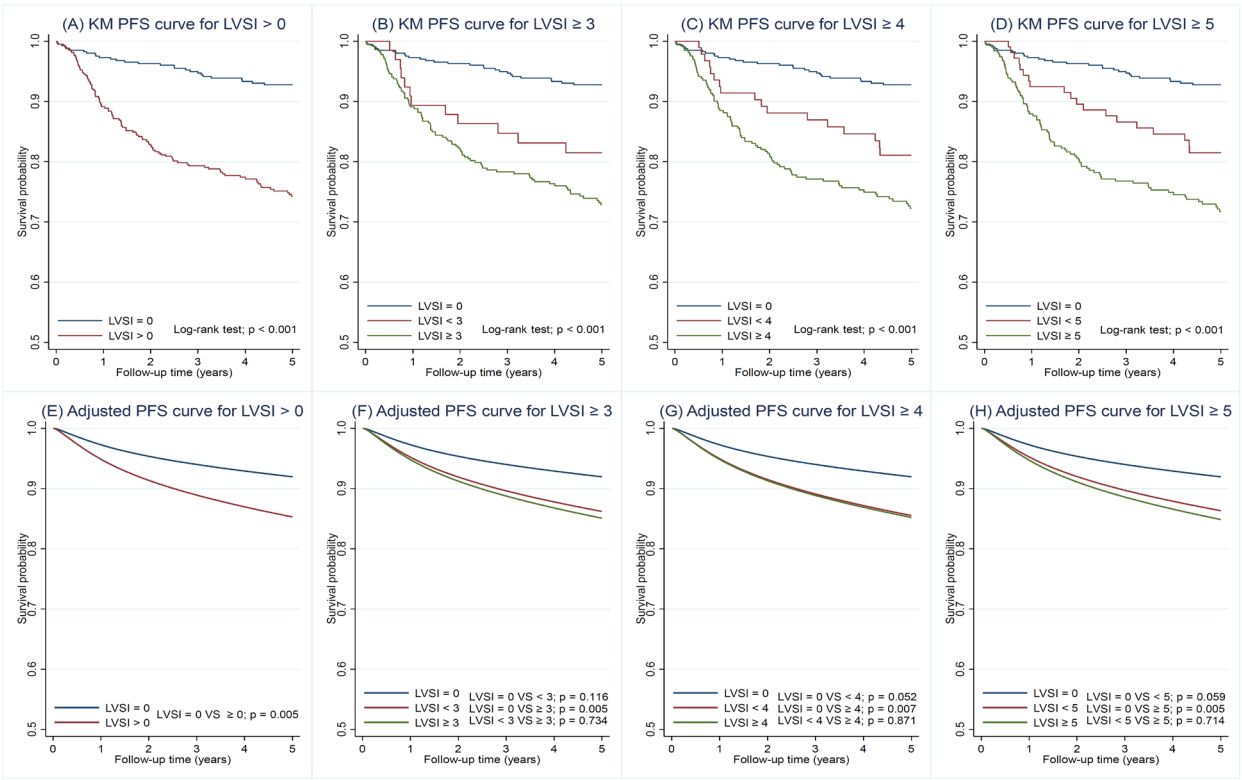

Figure 1. Survival Curves for Progression-Free Survival (PFS). (A–D) Kaplan–Meier curves for LVSI status and different cut-off values (3, 4, and 5 spaces). (E–H) Adjusted survival curves from flexible parametric survival models. Numbers of patients in each comparison were as follows: (A, E) LVSI = 0 (n=410) vs >0 (n=433); (B, F) LVSI = 0 (n=410), <3 (n=68), ≥3 (n=365); (C, G) LVSI = 0 (n=410), <4 (n=98), ≥4 (n=335); (D, H) LVSI = 0 (n=410), <5 (n=114), ≥5 (n=319).

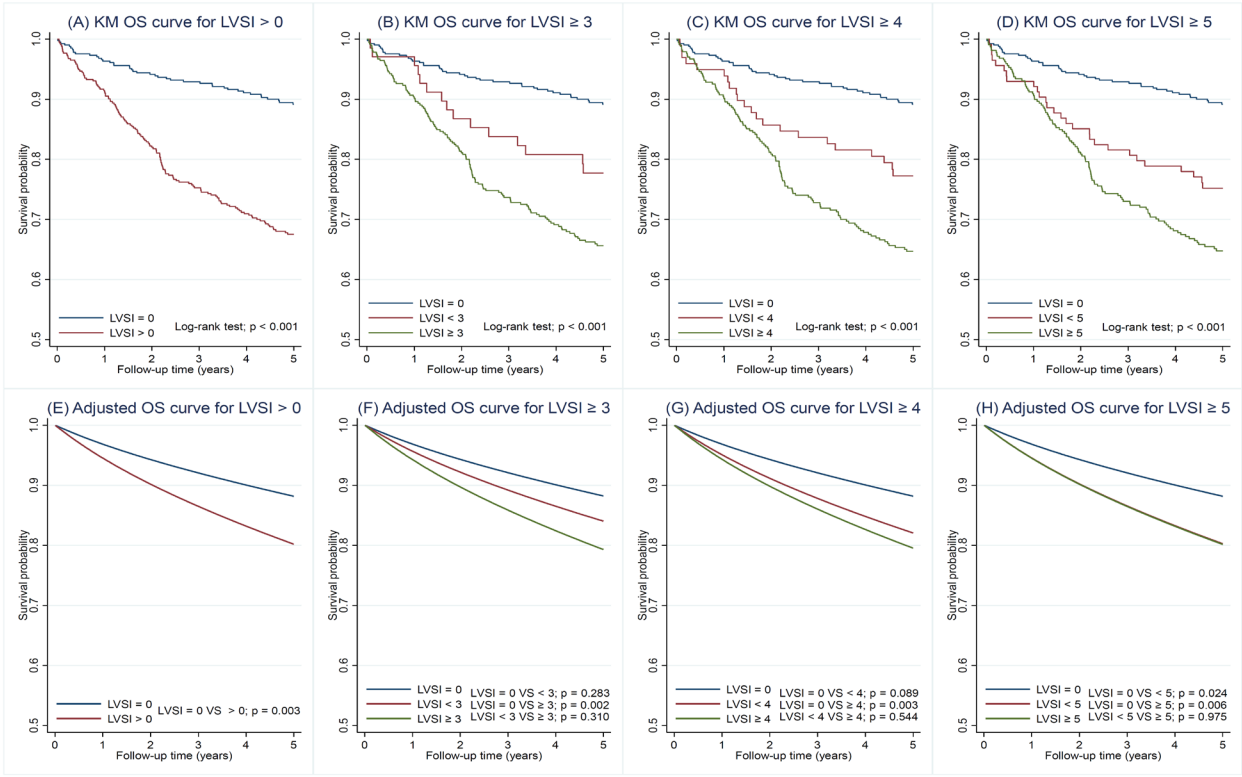

Figure 2. Survival Curves for Overall Survival (OS). (A–D) Kaplan–Meier curves for LVSI status and different cut-off values (3, 4, and 5 spaces). (E–H) Adjusted survival curves from flexible parametric survival models. Numbers of patients in each comparison were as follows: (A, E) LVSI = 0 (n=410) vs >0 (n=433); (B, F) LVSI = 0 (n=410), <3 (n=68), ≥3 (n=365); (C, G) LVSI = 0 (n=410), <4 (n=98), ≥4 (n=335); (D, H) LVSI = 0 (n=410), <5 (n=114), ≥5 (n=319).

LVSI (adjusted HR 1.89, 95%CI 1.21-2.96, p = 0.005). The substantial LVSI groups (≥3, ≥4, or ≥5 spaces) demonstrated significantly poorer adjusted PFS compared to the absent LVSI group (p = 0.005–0.007). Focal LVSI groups showed a trend toward lower adjusted PFS compared with the absent LVSI group (Figure 1F–H), although the differences were not statistically significant (p = 0.116, 0.052, and 0.059 for LVSI 1–2, 1–3, and 1–4 spaces, respectively). Adjusted PFS did not differ significantly between the focal and substantial LVSI groups (p = 0.714–0.871; Figure 1F–H).

For the 5-year adjusted OS, patients with LVSI had significantly poorer survival than those without LVSI (adjusted HR 1.75, 95%CI 1.20-2.56, p = 0.003). Substantial LVSI was associated with worse adjusted OS compared to absent LVSI (p = 0.002–0.006). Focal LVSI, as defined by 1-4 spaces, was also associated with poorer adjusted OS compared to absent LVSI (p = 0.024). No significant OS difference was found between focal and substantial LVSI groups (p = 0.310–0.975; Figure 2F–H).

Discussion

The results reflect real-world clinical practice, in which LVSI quantification was included in surgical pathology reports and used to guide clinical management. In this study, the clinical and pathological differences between the non-aggressive and aggressive histology groups align with existing literature [12, 13]. LVSI was a predictor of decreased PFS and OS.

Considering the 5-year adjusted progression risk, the presence of LVSI significantly increased the risk from 9.1% in patients without LVSI to 13.8% (Table 3). Notably, there was only a slight variation in adjusted progression risk, reaching 14.4% when LVSI cut-off values was increased to 10 spaces. The finding further supports the notion that the detection of any LVSI has a significant impact on disease progression, while the risk difference based on LVSI quantity is less pronounced. The prognostic impact of focal LVSI, as reported in other studies [10, 14, 15], warrants validation in further research.

In Kaplan-Meier plot analysis, each LVSI cut-off value further stratified risk levels among the EC patients with LVSI. The finding aligns with the traditional classification of LVSI quantity in EC patients into 3 categories (absent, focal, and substantial) [3, 16, 17], although the absent and focal LVSI categories are currently combined into the same low-risk group [2, 9]. After adjusting for the independent risk factors for survivals, the presence of LVSI remained associated with poorer adjusted PFS and OS. Patients with substantial LVSI (at least 3 spaces) had significantly worse adjusted PFS and OS compared to those without LVSI. Patients with focal LVSI (<3-5 spaces) showed a trend toward inferior adjusted PFS and OS compared with the LVSI-negative group. Importantly, a significant difference in adjusted OS was observed between patients with LVSI <5 spaces and those without LVSI (p=0.024), suggesting that a cut-off of fewer than 5 spaces for focal LVSI may be more appropriate. Additionally, no significant differences in adjusted survivals were observed between the focal LVSI and substantial LVSI groups. These findings are consistent with the results of a recent large study on stage I EC patients with non-aggressive histology [10], which showed no significant clinical outcome differences between patients with focal LVSI and those with substantial LVSI. Further information from real-world studies across different regions are needed to confirm the prognostic significance of focal LVSI, which could potentially refine the threshold for justifying adjuvant treatment and improve clinical outcomes in low-stage EC patients.

The strength of this study is that it represents the real-world application of LVSI quantification as a part of pathological reporting for EC patients. The single-institution setting facilitated the implementation of a consistent policy for managing EC patients in alignment with the guidelines available at the time. The results and clinical outcomes were also statistically adjusted for multiple risk parameters.

Several limitations in this study should be addressed. First, the data were derived from a retrospective collection of reported pathological and clinical information. Second, survival comparisons among focal LVSI categories were part of an exploratory objective; therefore, no formal a priori sample size calculation was performed for LVSI categorization with respect to the survival endpoint. However, given the number of patients and events within each group, the analyses were considered to be sufficiently powered. Finally, incomplete follow-up data on recurrence status and the lack of disease-specific mortality information may have introduced information bias.

In conclusion, substantial LVSI (at least 3 involved spaces) is strongly associated with poorer prognosis in EC. Additionally, focal LVSI may be associated with decreased survival. These findings underscore the prognostic value of LVSI quantification and support further investigation into the clinical relevance of focal LVSI.

Author Contribution Statement

TP: Conceptualization, data collection, formal analysis, data interpretation, manuscript writing, and editing. PW: Conceptualization, data collection, data interpretation, manuscript review, and editing. PP and NS: Data interpretation, manuscript writing, and editing. CC, KS, JS, and SS: Data collection, manuscript review, and editing. SK: Conceptualization, data collection, formal analysis, data interpretation, manuscript writing, and editing. .

Acknowledgements

Ethical issue

The study was approved by the Institution Review Board (IRB), Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (IRB No. PAT-2565-0059).

Conflict of interest statement

The authors declare no conflict of interest.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. https://doi.org/10.3322/caac.21492.
2. Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet. 2023;162(2):383-94. https://doi.org/10.1002/ijgo.14923.
3. Bosse T, Peters EE, Creutzberg CL, Jurgenliemk-Schulz IM, Jobsen JJ, Mens JW, et al. Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer--a pooled analysis of PORTEC 1 and 2 trials. Eur J Cancer. 2015;51(13):1742-50. https://doi.org/10.1016/j.ejca.2015.05.015.
4. Qian Y, Pollom EL, Nwachukwu C, Seiger K, von Eyben R, Folkins AK, et al. Extent of lymphovascular space invasion may predict lymph node metastasis in uterine serous carcinoma. Gynecol Oncol. 2017;147(1):24-9. https://doi.org/10.1016/j.ygyno.2017.07.119.
5. Fujimoto T, Nanjyo H, Fukuda J, Nakamura A, Mizunuma H, Yaegashi N, et al. Endometrioid uterine cancer: Histopathological risk factors of local and distant recurrence. Gynecol Oncol. 2009;112(2):342-7. https://doi.org/10.1016/j.ygyno.2008.10.019.
6. Matias-Guiu X, Anderson L, Buza N, Ellenson LH, Fadare O, Ganesan R, et al. Endometrial cancer histopathology reporting guide. International Collaboration on Cancer Reporting. 5th ed. Sydney, Australia; 2024.
7. National Comprehensive Cancer Network. NCCN Guidelines Version 2.2024: Uterine Neoplasms. Plymouth Meeting, PA: National Comprehensive Cancer Network; 2024.
8. Turashvili G, Karnezis AN, Crothers BA, Krishnamurti UG, McCluggage G, Rabban J, Soslow R. Protocol for the examination of Specimens from patients with Carcinoma of the Endometrium. College of American Pathologists: Northfield, IL, USA. 2024.
9. Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Int J Gynecol Cancer. 2021;31(1):12-39. https://doi.org/10.1136/ijgc-2020-002230.
10. Dagher C, Bjerre Trent P, Alwaqfi R, Davidson B, Ellenson L, Zhou QC, et al. Oncologic outcomes based on lymphovascular space invasion in node-negative FIGO 2009 stage I endometrioid endometrial adenocarcinoma: A multicenter retrospective cohort study. Int J Gynecol Cancer. 2024;34(10):1485-92. https://doi.org/10.1136/ijgc-2024-005746.
11. Bhatnagar AR, Ghanem AI, Alkamachi B, Allo G, Lin CH, Hijaz M, et al. The prognostic impact of substantial lymphovascular space invasion in women with node-negative FIGO stage I uterine carcinoma. Gynecol Oncol. 2024;188:44-51. https://doi.org/10.1016/j.ygyno.2024.06.009.
12. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic oncology group study. Cancer. 1987;60(8 Suppl):2035-41. https://doi.org/10.1002/1097-0142(19901015)60:8+<2035::aid-cncr2820601515>3.0.co;2-8.
13. Barlin JN, Soslow RA, Lutz M, Zhou QC, St Clair CM, Leitao MM Jr, et al. Redefining stage I endometrial cancer: Incorporating histology, a binary grading system, myometrial invasion, and lymph node assessment. Int J Gynecol Cancer. 2013;23(9):1620-8. https://doi.org/10.1097/IGC.0b013e3182a5055e.
14. Blinman P, Mileshkin L, Khaw P, Goss G, Johnson C, Capp A, et al. Patients' and clinicians' preferences for adjuvant chemotherapy in endometrial cancer: An ANZGOG substudy of the PORTEC-3 intergroup randomised trial. Br J Cancer. 2016;115(10):1179-85. https://doi.org/10.1038/bjc.2016.323.
15. Peters EEM, Leon-Castillo A, Smit V, Boennelycke M, Hogdall E, Hogdall C, et al. Defining substantial lymphovascular space invasion in endometrial cancer. Int J Gynecol Pathol. 2022;41(3):220-6. https://doi.org/10.1097/PGP.0000000000000806.
16. Barnes EA, Martell K, Parra-Herran C, Taggar AS, Donovan E, Leung E. Substantial lymphovascular space invasion predicts worse outcomes in early-stage endometrioid endometrial cancer. Brachytherapy. 2021;20(3):527-35. https://doi.org/10.1016/j.brachy.2020.12.006.
17. Pifer PM, Bhargava R, Patel AK, Ling DC, Vargo JA, Orr BC, et al. Is the risk of substantial LVSI in stage I endometrial cancer similar to PORTEC in the North American population? A single-institution study. Gynecol Oncol. 2020;159(1):23-9. https://doi.org/10.1016/j.ygyno.2020.07.024.