The impact of lymphovascular space invasion on recurrence and survival rate among women with stage I endometrioid endometrial cancer

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ABSTRACT

Introduction: Endometrial cancer is the most common gynecologic malignancy in developed countries, with rising incidence worldwide. While early stage disease generally carries a favorable prognosis, recurrence remains a significant clinical concern. Among the histopathological features, lymphovascular space invasion (LVSI) has emerged as a critical prognostic factor, reflecting tumor aggressiveness and potential for metastatic spread. LVSI is associated with increased risk of recurrence, distant metastasis, and reduced survival, even in patients with otherwise low risk disease. Understanding the role of LVSI in endometrial cancer is essential for refining risk stratification, guiding adjuvant therapy decisions, and improving patient outcomes. Our study to evaluate the impact of lymphovascular space invasion (LVSI) on treatment outcomes, recurrence, and survival in patients with stage I endometrioid endometrial cancer.

Materials and Methods: A retrospective cohort study was conducted at the Hospital Canselor Tuanku Muhriz (HCTM) Gynecologic Oncology Clinic, with ethical approval from Universiti Kebangsaan Malaysia. Patients with stage I endometrial carcinoma, classified according to the International Federation of Gynecology and Obstetrics (FIGO) 2018, and confirmed on hysterectomy specimens were included. Demographic clinicopathological, and treatment data were collected. LVSI was defined as the presence of tumor cells within endothelial lined spaces. Overall survival (OS) was the primary endpoint. Statistical analyses were performed using SPSS version 26, employing chi square, t tests, and Kaplan–Meier estimates, with significance set at $p < 0.05$.

Results: Of 180 patients, 163 had endometrioid carcinoma; 114 were included in the final analysis (mean age 58 years; 79.8% postmenopausal). LVSI was present in 14.2% of cases and was associated with higher grade and deeper myometrial invasion. Recurrence occurred in 8.5% overall, with 18.8% in LVSI positive and 4.1% in LVSI negative patients. The 2 year disease free survival (DFS) rate was 93.4% (80.8% LVSI positive vs 99% LVSI negative). The 5 year DFS rate was 91.1% (73.4% LVSI positive vs 94% LVSI negative). The OS rate was 97.3% (87.5% LVSI positive vs 99% LVSI negative). Distant metastasis predicted 2 year DFS, whereas LVSI positivity independently predicted reduced 5 year OS. At 5 years, the DFS rate was 91.1% (SE = 0.031), while the OS rate was 97.3% (SE = 0.013). The similarity between DFS and OS reflects the low number of recurrence and death events, indicating favorable prognosis and effective disease control. Median survival was not reached.

Conclusion: LVSI was associated with higher recurrence and poorer survival in patients with Stage I endometrioid endometrial carcinoma, independently predicting 5-year survival, supporting its role in risk stratification and treatment planning.

KEYWORDS:
Endometrial carcinoma; carcinoma, endometrioid; recurrence; survival rate; prognosis

INTRODUCTION

Endometrial cancer (EC) is the fifteenth most common malignancy worldwide and the sixth most common malignancy in women.[1] According to the International Agency for Research on Cancer (IARC), approximately 420,368 new cases of EC were diagnosed, and approximately 97,273 deaths were attributed to the disease in 2022.[1]

In Malaysia, EC ranks higher than global rates, being the fifth most common cancer in the country. According to IARC, approximately 1503 new cases of EC and 458 deaths were reported in Malaysia in 2022.[1] According to the Malaysian National Cancer Registry, the lifetime risk for uterine malignancy is one in 127 for all females, and 48.6% of cases are diagnosed at stage I.[2] The most significant risk factors associated with EC development are those that increase long-term exposure to unopposed estrogen (e.g., obesity and exogenous estrogen).[3]

Generally, patients with EC have a relatively favorable outcome.[4] Most patients present with International Federation of Gynecology and Obstetrics (FIGO) stage I

This article was accepted: 24 June 2026
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endometrioid cancers and do not have lymph node metastases at surgical staging. Despite uterine-limited disease on final pathology, 10–20% of these cancers recur.[5-7] Relapse usually occurs within 24 months of diagnosis.[5-7] Many studies report that young women with endometrial carcinoma tend to have a prognostically favorable histological type, such as endometrioid-type tumor, well-differentiated tumor grading, early staging, less myometrial involvement, and absence of lymphovascular stromal invasion.[4,7-9] This reflects the relatively good prognosis of EC when detected early or at a younger age.

The incidence is highest in the 55-69 age group, and an increased rate is seen in most age groups in 2017-2021.[2] Clinicopathological factors such as older age, deep myometrial invasion, grade 3 disease, and lymphovascular space invasion (LVSI) have predictive value for tumor recurrence and worse survival.[4]

LVSI is present in approximately 15% of early-stage ECs and is considered a potential adverse prognostic factor in EC. Researchers have found that patients with LVSI positivity show a higher rate of lymph node metastasis (LNM), are more likely to have local or distal relapses, and usually have shorter overall survival (OS).[10-17]

The Cancer Genome Atlas (TCGA) publication in 2013 decoded endometrial cancer into four expanded subtypes as they have their characteristics, molecular features, and prognosis.[1]

POLE ultra-mutated is characterized by a strong association with mutations in the exonuclease domain of polymerase-ε *(POLE)*, a group of tumours with a good prognosis that could exclude the necessity of adjuvant treatment.[2] Microsatellite instability (MSI) hypermutated is characterized by a loss of DNA mismatch repair proteins (MLH1, MSH2, MSH6, and PMS2). (3)Copy-number high, with *TP53* mutations, is usually associated with unfavourable results/poor prognosis, and (4) copy-number low with microsatellite stability and intermediate prognosis.[18-20]

The information brought by the molecular biology of EC may be relevant as a tool for predictive assessment and in the definition of therapeutic strategies, and the new FIGO 2023 document supports its incorporation in its staging system, despite controversies.[21] According to the new FIGO staging, in cases of anatomical stage I–II, the detection of a *POLE* mutation currently results in a decrease in the FIGO stage.[21] At the same time, abnormal p53 leads to increased staging, yielding escalation or de-escalation of adjuvant treatment. Furthermore, in cases of advanced disease, molecular types and their associations with hormonal expression, loss of expression of repair enzymes, and overexpression of HER2 are also valuable for choosing therapies. Several studies, including Gynecology Oncology Group (GOG) 99 and the Post-Operative Radiation Therapy in Endometrial Carcinoma (PORTEC) one and two randomized trials, found that patients with early-stage EC and LVSI treated with external beam radiation therapy (EBRT) had a decreased risk of pelvic recurrence without significant improvement in OS.[7,11,22-23] Based on these findings, Bosse et al. recommended the consideration of adjuvant EBRT in patients with early-stage EC and substantial LVSI, especially in the presence of additional risk factors.[11] The American National Comprehensive Cancer Network (NCCN) guideline, the American College of Obstetricians and Gynecologists/ Society of Gynecologic Oncology (ACOG/SGO) guideline, the European Society for Medical Oncology (ESMO), the European Society of Gynecological Oncology (ESGO), the European Society of Radiotherapy and Oncology (ESTRO) guideline, and the International Federation of Gynecology and Obstetrics (FIGO) for EC all consider LVSI and molecular classification as a risk factor and recommend LVSI-positive early-stage patients to receive adjuvant therapy after surgery.[9,24-25] Nevertheless, in recent years, some studies from different countries have shown negative results regarding the prognostic role of LVSI.[26-30] This reflects the ongoing debate on LVSI as a predictor of EC prognosis and the efficacy of adjuvant therapy in such cases. We aimed to explore the impact of LVSI on recurrence and survival rates in EC stage I patients in Malaysia.

MATERIALS AND METHODS

This retrospective cohort study was conducted at the Gynecologic Oncology Clinic of Hospital Canselor Tuanku Muhriz (HCTM), a tertiary referral centre in Malaysia. Ethical approval was obtained from the Research Ethics Committee of the National University of Malaysia (RECUKM), and the study adhered to the principles of the Declaration of Helsinki.

All patients diagnosed with endometrial carcinoma and managed at HCTM between January 2002-December 2024 were reviewed. The study population was restricted to women with Stage I disease, classified according to FIGO 2018 staging system. Staging was confirmed by the final histopathological examination of the hysterectomy specimens following total abdominal hysterectomy with bilateral salpingo-oophorectomy and omental biopsy. Pelvic and para aortic lymphadenectomy was performed in most cases based on the surgeon's discretion and intraoperative findings. Patients with incomplete records, synchronous malignancies, or prior neoadjuvant therapy were excluded from the study.

Clinical and pathological data were extracted from electronic medical records and pathological reports. The demographic variables included age at diagnosis, ethnicity, menopausal status, parity, and comorbidities (e.g., hypertension and diabetes mellitus). Tumour characteristics included histological grade, tumour size, depth of myometrial invasion, presence of LVSI, and involvement of the lower uterine segment. Adjuvant treatment modalities (brachytherapy, external beam radiotherapy, or chemotherapy) were determined by the multidisciplinary team on stage, histologic grade, LVSI, and patient age. External beam radiotherapy (EBRT) was administered to high risk patients at a total dose of 45 Gy in 25 fractions over 5 weeks, with concurrent weekly cisplatin (40 mg/m^2) as a radiosensitizer, followed by high dose rate (HDR) brachytherapy at 5.5 Gy in 2 fractions. Vaginal vault brachytherapy was prescribed for intermediate risk patients at 21 Gy to 5 mm depth in 3 fractions over 2–3 weeks. Patients in the observation group did not receive adjuvant

therapy. These treatment strategies were applied in accordance with the Royal College of Radiologists (RCR) recommendations, ensuring alignment with contemporary standards of care.

LVSI was defined as the presence of viable tumour cells within endothelial lined lymphatic or vascular spaces beyond the main tumour mass, as identified on haematoxylin and eosin–stained sections. A general pathologist reviewed the histopathological slides. In keeping with the retrospective design of the study, LVSI status was recorded as either present or absent, without further subcategorization of extent or severity. The primary endpoint was OS, which was measured from the date of surgery to death from any cause. Patients alive at the last follow-up were censored on that date. The secondary endpoints included recurrence patterns and disease-free survival at 2 and 5 years (DFS), where available. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) Statistics version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as means ± standard deviations or medians with interquartile ranges, depending on the distribution, and compared using independent t-tests or Mann–Whitney U tests, as appropriate. Categorical variables were expressed as frequencies and percentages, and group differences were assessed using the chi-square or Fisher's exact tests. Survival probabilities at two and five years were estimated using the Kaplan–Meier method, and differences between strata were evaluated using the log-rank test. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to estimate the hazard of recurrence. Univariate analysis used to estimate hazard ratios (HRs) for each factor separately to identify independent predictors of survival, with variables significant at $p<0.05$. Cox regression analysis for variables meeting the selection threshold ($p<0.05$) was entered into further evaluation. For each factor, hazard ratios (HRs) with 95% confidence intervals (CIs) were reported. Statistical significance was defined as $p<0.05$.

RESULTS

A total of 180 patients with Stage I endometrial carcinoma were reviewed. Of these 163 (90.6%) with endometrioid carcinoma identified, 114 fulfilled the predefined inclusion criteria and were included in the final analysis, while the remaining 49 were excluded. The mean age at diagnosis was 58.1 years (Standard Deviation (SD)=10.14), and the majority were postmenopausal (79.8%). The most common comorbidities were hypertension (14.9%), diabetes mellitus (2.6%), and dyslipidaemia (6.1%). The details of the study parameters are presented in Table I.

Within the cohort, 54.4% were classified as Stage IA, 40.4% as Stage IB, and 5.3% as Stage IC, according to FIGO 2018 criteria. Histological grading revealed 61.4% of tumours were Grade I, 29.4% Grade II, and 8.8% Grade III. LVSI was identified in 14% of the cases. Table II presented the details of study parameters in both LVSI-negative and LVSI-positive groups

Among LVSI positive patients, 68.8% received adjuvant therapy and 31.3% were managed with observation alone. In contrast, among LVSI negative patients, 19.4% received adjuvant therapy and 80% were managed conservatively. The decision regarding the modalities of adjuvant therapy was determined by a multidisciplinary team, based on the stage, histological grade, LVSI and the patient age.

Recurrence was radiologically and histologically confirmed. Overall, 7.9% of the patients experienced disease recurrence. Recurrence was significantly more frequent in LVSI-positive cases (18.8%) than in LVSI-negative cases (4.1%). The sites of recurrence included distant metastasis (n=5; 2 LVSI-positive, 3 LVSI-negative), locoregional recurrence (n=2; 1 LVSI-positive, 1 LVSI-negative), and abdominal recurrence (n=; 1 1 LVSI-negative).

For the entire cohort, the mean time to recurrence was 58.2 months (95% CI, 56.7–59.8). Kaplan–Meier analysis showed that the median time to recurrence was not reached in either subgroup, as fewer than 50% of patients experienced recurrence. The mean time to recurrence was 59.2 months (95% CI: 58.2–60.3) for LVSI negative patients and 52.2 months (95% CI: 41.0–58.7) for LVSI positive patients. These findings indicate that recurrence occurred earlier and more frequently in LVSI positive patients compared to LVSI negative patients.

The median disease free survival (DFS) was not reached, as fewer than 50% of patients experienced recurrence or death during follow up. Patients lost to follow up were censored at their last disease free visit, contributing survival information up to that point. The estimated 2 year DFS rate for the entire cohort was 93.4% (95% CI, 92.9–99.9), with a mean DFS of 23.8 months (95% CI, 23.5–24.1). At 5 years, the estimated DFS rate was 91.1% (95% CI, 85.4–96.8), with a mean DFS of 57.9 months (95% CI, 56.2–59.6), as derived from the Kaplan–Meier survival function. Subgroup analysis revealed that patients with LVSI negative tumours had superior outcomes, with 2 year and 5 year DFS rates of 99% and 94%, respectively, whereas LVSI positive patients demonstrated poorer survival, with corresponding DFS rates of 80.8% and 73.4%. Univariate Cox proportional hazards regression demonstrated that LVSI was significantly associated with Disease free survival. The hazard ratio was 6.439 (95% CI: 1.721–24.082), indicating that patients with LVSI positive tumours had more than a six fold increased risk of recurrence and death compared to those without LVSI. These findings are illustrated in Figure 1.

Overall survival outcomes were similarly favourable. For the cohort of 114 patients, survival remained stable, with 2 year and 5 year OS rates of 97.3% (95% CI, 94.2–100.0). Stratified by LVSI status, the 2 year and 5 year OS was 99% in LVSI negative patients compared to 87.5% (95% CI, 69.1–100.0) in LVSI positive patients, with only three deaths occurred within the first 2 years, and no additional events were observed thereafter. However, because some patients were lost to follow up, it cannot be confirmed with certainty that these were the only deaths within the study cohort. These findings are illustrated in Figure 1. These findings highlight LVSI as an adverse prognostic factor for long term survival.

Table I: Baseline Characteristics of Stage I Endometrial Carcinoma Patients

Parameter	Frequency	Percentage %
Histological subtypes		
Endometrioid	163	90.60%
Serous	5	2.80%
Mixed	2	1.10%
Carcinosarcoma	5	2.80%
Mucinous	2	1.10%
Clear	1	0.60%
Not documented	2	1.10%
Ethnicity		
Malay	63	55.30%
Chinese	38	33.30%
Indian	9	7.90%
Other	4	3.50%
Menopausal Status		
Perimenopause	23	20.2%
Post menopause	91	79.8%
Tumour Stage		
STAGE1A	62	54.40%
STAGE1B	46	40.40%
STAGE1C	6	5.30%
Tumour Grade		
Grade I	70	61.40%
Grade II	34	29.40%
Grade III	10	8.80%

Survival rates stratified by LVSI status and adjuvant therapy demonstrated that LVSI positive patients without adjuvant therapy had lower survival compared to LVSI negative patients (80% vs. 99%, p<0.004). With brachytherapy alone, 5 year survival was 80% in LVSI positive versus 100% in LVSI negative patients (p=0.031). EBRT plus brachytherapy (100% vs 100%, p=0.44) were comparable between groups. In contrast, concurrent chemoradiotherapy was associated with poorer survival in both LVSI positive and LVSI negative patients (50% each, p=0.05) The details of the comparison of various adjuvant therapies according to LVSI status are presented in Table III.

Univariate analysis identified several clinicopathological variables with significant impact on OS. Patients with hypertension and dyslipidaemia had markedly poorer outcomes (non survivors 28.6% vs survivors 71.4%, p<0.001). Stage IB disease was associated with reduced survival (p=0.035), while Grade 1 tumours were linked to favourable prognosis (100% survival, p=0.025). Depth of invasion was significant, with invasion <50% showing 100% survival (p=0.011) compared to invasion >50% (90.9% survival, p=0.006). LVSI positivity was also associated with adverse outcomes (87.5% survival vs 12.5% non survivors, p=0.006). Treatment modality influenced survival, with concurrent chemoradiotherapy (CCRT) showing poorer outcomes (50% survival, p<0.001). Recurrence (p=0.001) and distant metastasis (p<0.001) were strongly associated Table IV presents the factors significantly impacting OS rates in the univariate analysis.

DISCUSSION

This retrospective cohort study evaluated the prognostic significance of LVSI in patients with Stage I endometrioid endometrial carcinoma. Our findings demonstrate that LVSI is significantly associated with increased recurrence and reduced survival, underscoring its role as a key prognostic factor in early-stage disease.

The LVSI-positive rate of 14% in our cohort is consistent with previously reported ranges (8.3–32.8%).[11,27-31] Dai et al. for example, reported a rate of 12.16% [31], while Tortorella et al. observed higher frequencies in certain subgroups.[32] Variability across studies likely reflects differences in LVSI definition, pathologic assessment, and patient selection criteria, highlighting the need for standardized reporting of these parameters.

The overall recurrence rate in our study was 8.5%, but recurrence was disproportionately higher among LVSI-positive patients (18.8%) compared to LVSI-negative patients (4.1%). This aligns with the findings of Ureyen et al. who identified LVSI as an independent predictor of recurrence,[34] and Restaino et al. who demonstrated its association with both recurrence and distant metastasis.[32]

LVSI was also significantly associated with decreased survival rates. LVSI-positive patients had poorer outcomes. Kaplan–Meier analysis confirmed these differences, with statistically significant reductions in both Disease-free survival (χ^2=10.388, p<0.001) and OS (χ^2=7.441, p=0.006). These findings are consistent with those of Qin et al. (2023), whose meta-analysis demonstrated that LVSI is a strong predictor of recurrence (OR=2.79), reduced OS (HR=5.19), and reduced recurrence-free survival (HR=5.26). Similarly, Tortorella et al. reported a reduction in 5 year OS from 99.5% to 70.6% and in DFS from 93.6% to 56.5% among LVSI-positive patients.[32] Ureyen et al. also noted a decline in DFS from 96.8% to 80.1%.[34] In contrast, Askandar et al. and Dai et al. did not find LVSI to be an independent prognostic factor in multivariate analyses, suggesting that sample size, adjuvant therapy practices, and confounding variables may explain discrepancies across studies.[31,35]

Table II: Study parameters in the LVSI-negative and LVSI-positive groups

Parameter	LVSI-negative n (%)	LVSI-positive n (%)	p-value
Mean age ± SD	58.28 ± 9.917	56.30 ± 11.649	0.50
Mean Parity	2.47 ± 1.949	2.38 ± 2.062	0.98
Menopausal status			0.60
Post menopause	79(80.6%)	12(75%)	
Perimenopause	19(19.4%)	4(25%)	
Comorbidity			
Diabetes mellitus	3(3.1 %)	0(0%)	0.48
Hypertension	16(16.3%)	1(6.3%)	0.29
Dyslipidaemia	5(5.1%)	1(6.3%)	0.98
Hypertension and diabetes mellitus	16(16.3%)	5(31.3%)	0.15
Diabetes mellitus and Dyslipidaemia	8 (8.2%)	2(12.5%)	0.57
Diabetes mellitus, hypertension and Dyslipidaemia	14(14.3%)	1(6.3%)	0.38
Myometrial invasion			
< 50%	69(70.4%)	7(43.4%)	0 .061
> 50%	25(25.5%)	9(56.3%)	0.022
Absence of myometrial invasion	4(4.1%)	0 (0%)	
No adjuvant therapy	79(80.6%)	5(31.3%)	<0.001
Adjuvant therapy	19(19.4%)	11(68.8%)	<0.001
Vaginal brachytherapy	13(13.3%)	5(31.3%)	
Vaginal brachytherapy and EBRT	4(4.1%)	4(25%)	0.010
CCRT	2(2%)	2(12.5%)	
Stage			0.007
IA	59(60.2%)	3(18.8%)	0.002
IB	34(34.7%)	12(75%)	0.002
IC	5(5.1%)	1(6.3%)	0.890
Grade			
I	62(63.3%)	8(50%)	0.312
II	28(28.6%)	6(37.5%)	0.469
III	8(8.2%)	2(12.5%)	0.570
Lymphadenectomy			0.7
No Lymphadenectomy	30(30.6%)	6(37.5%)	
Pelvic Lymphadenectomy	68(69.4%)	10(62.5%)	
Recurrence	5(4.1%)	3(18.8%)	0.002
Recurrence site			
Locoregional	1(1%)	1(6.3%)	0.79
Abdominal	1(1%)	0(0%)	0.72
Distant	3(3.1%)	2(12.5%)	0.05
Mean time to Recurrence (Months)	59.2 months	52.2 months	0.006
2-year Disease Free Survival	99%	80.8%	<0.001
5-year Disease Free Survival	94%	73.4%	0.006
Overall survival	97(99%)	14 (87.5%)	0.005

LVSI, lymphovascular space invasion. EBRT, external beam radiotherapy. CCRT, concurrent chemoradiotherapy. SD: standard deviation. Statistical significance was set at p<0.05.

Table III: Survival rates based on adjuvant therapies in LVSI-negative and LVSI-positive groups

Parameter	LVSI-positive	LVSI-negative	p-value
No adjuvant	5(80%)	79(98.8%)	0.04
Brachytherapy	4(80%)	12(100%)	0.32
EBRT+ Brachytherapy	4(100%)	5(100%)	0.44
CCRT	2(50%)	2(50%)	0.05

LVSI, lymphovascular space invasion; EBRT, external beam radiotherapy. CCRT, concurrent chemoradiotherapy Statistical significance was set at p<0.05.

Table IV: Factors with significant impact on OS rate in univariate analysis

Parameter	Non-survivors	Survivors	p-value
Hypertension and dyslipidaemia	2(28.6%)	5(71.4%)	<0.001
Stage IB	3(6.5%)	43(93.5%)	0.035
Grade 1	0(0%)	70(100%)	0.025
Invasion<50%	0(0%)	77(100%)	0.011
Invasion>50%	3(9.1%)	30.(90.9%)	0.006
Positive LVSI	2(12.5%)	14(87.5%)	0.006
CCRT	2(50%)	2(50%)	<0.001
Recurrence	2(20%)	8(80%)	0.001
Distant metastasis	2(40%)	3(60%)	<0.001

LVSI, lymphovascular space invasion; EBRT, external beam radiotherapy. CCRT, concurrent chemoradiotherapy. Statistical significance was set at p<0.05.

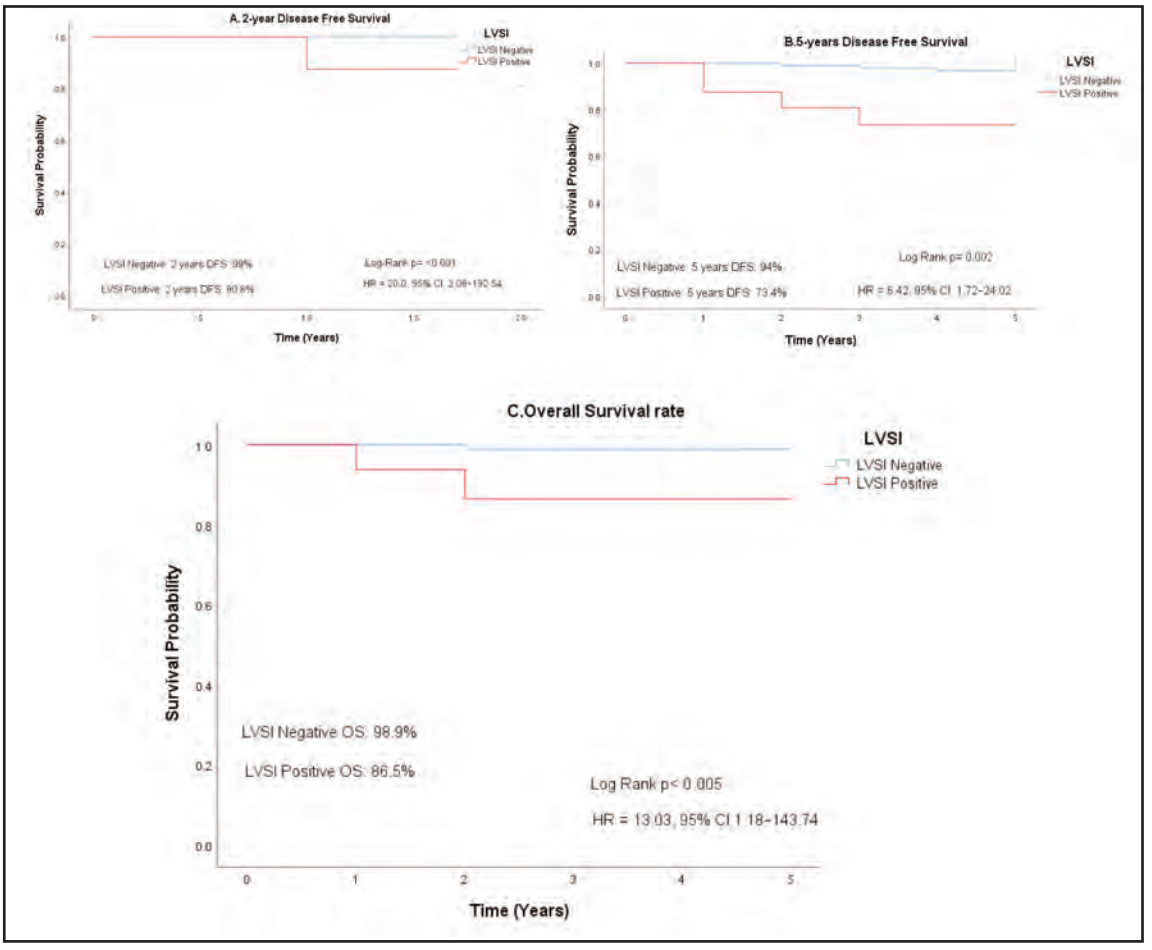

Fig. 1: A two-year disease-free survival; B, five-year disease-free survival; C, overall survival. DFS, disease-free survival; OS, overall survival; LVSI, lymphovascular space invasion

In our cohort, LVSI correlated with a higher deeper myometrial invasion, and greater use of adjuvant chemotherapy (68.8% vs. 19.4% in LVSI-negative cases). These associations are consistent with prior reports linking LVSI to aggressive pathological features.[32] Despite the more frequent use of chemotherapy in LVSI-positive patients, recurrence rates did not differ significantly between the treated and untreated subgroups ($p>0.05$). This may reflect the limited sample size and event numbers, but it also raises questions about the adequacy of current adjuvant strategies in mitigating LVSI-related risk. The lack of survival benefit in the multivariate analysis suggests that LVSI may identify a biologically aggressive subset of tumours that are less responsive to conventional therapies.

Although OS was defined as time from surgery to death from any cause, the available follow-up and number of death events limited the precision of longer-term estimates; therefore, survival results are presented primarily as 5-year OS estimates. Additionally, molecular staining (e.g., POLE, p53-abnormal, MMRd) was not consistently available, precluding the evaluation of its prognostic role.

The findings of this study contribute to the growing body of evidence supporting LVSI as a clinically relevant prognostic marker. Nevertheless, limitations such as the retrospective design, single centre setting, modest sample size, and incomplete survival timing data must be acknowledged. These constraints underscore the need for validation in larger, prospective, multicentre studies with standardized pathological evaluation of LVSI. Importantly, future research should integrate molecular classification systems (The Cancer Genome Atlas / Proactive Molecular Risk Classifier for Endometrial Cancer or TCGA/ProMisE groups) in accordance with the ESGO/ESTRO/ESP 2023 recommendations, which emphasize the combined use of histopathological features and molecular profiles to refine risk stratification and guide individualized therapy. In clinical practice, LVSI positivity should also influence nodal assessment strategies: sentinel lymph node (SLN) mapping remains the preferred approach in apparent early stage endometrial cancer, but LVSI strengthens the rationale for performing nodal staging even in otherwise low risk cases. Incorporating LVSI status into decision making, alongside molecular classification, provides a more comprehensive framework for individualized management and ensures alignment with contemporary international standards.

CONCLUSION

This study demonstrates that LVSI is a significant and independent prognostic factor for Stage I endometrioid endometrial carcinoma. Its presence was strongly associated with increased recurrence, distant metastasis, and reduced OS, underscoring LVSI as a marker of aggressive tumour biology, even in early-stage disease. Importantly, LVSI correlated with adverse pathological features, such as deeper myometrial invasion, reinforcing its role as a surrogate indicator of poor prognosis.

From a clinical perspective, incorporating LVSI status into postoperative risk stratification provides an opportunity to refine the management strategies. Patients with LVSI-positive tumours may benefit from closer surveillance schedules and consideration of adjuvant therapy, whereas patients with LVSI-negative tumours could potentially avoid overtreatment. However, the lack of consistent survival benefit from chemotherapy in our cohort highlights the need for more targeted therapeutic approaches. LVSI may identify a biologically distinct subset of tumours that require novel systemic or combined modality treatments that go beyond conventional regimens.

In summary, LVSI should be recognized as a key determinant of outcome in Stage I endometrioid endometrial carcinoma. Its integration into risk stratification models with molecular classification system has the potential to optimize individualized management, improve prognostic accuracy, and guide future research on tailored adjuvant therapy strategies for early-stage EC.

CONFLICT OF INTEREST

All authors declare no financial or non-financial conflict of interest.

FUNDING

This research did not receive any special grant from funding agencies in the public, commercial, or not-for-profit sectors.

ETHICAL APPROVAL

This study was conducted in accordance with the Helsinki Declaration and was approved by Research Ethics Committee of the National University of Malaysia (IRB: JEP-2025-328).

DATA AVAILABILITY STATEMENT

Data is available upon request.

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