Nusantara Medical Science Journal
Volume 10, Issue 2, July – December 2025
P-ISSN: 2460-9757, E-ISSN: 2597-7288
Nationally Accredited Journal, Decree No. 230/E/KPT/2022.

Original Article

Clinicopathological Profile and Disease-Free Survival in Stage I-II Endometrial Cancer at Cipto Mangunkusumo Hospital

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ARTICLE INFO

Keywords:
endometrial cancer; disease-free survival; LVSI; tumor grade; prognosis; Indonesia.

How to cite:

DOI:

ABSTRACT

Introduction: *This study aimed to describe the clinicopathological profile and evaluate the disease-free survival (DFS) of patients with FIGO 2009 stage I–II endometrioid endometrial cancer, and to determine the prognostic value of key factors, emphasizing lymphovascular space invasion (LVSI) and tumor grade.* ***Methods****: A retrospective cohort of 111 patients treated between January 2017 and December 2022 was analyzed. Variables included age, menopausal status, BMI, depth of myometrial invasion, LVSI, and tumor grade. Survival was estimated using the Kaplan–Meier method; associations were assessed with Fisher's exact test, and independent prognostic factors were identified using multivariate Cox regression analysis* ***Results:*** *The median follow-up for the 111 patients was 32 months. Most were stage IB (42.4%), aged 45–60 years (46.8%), postmenopausal (73%), and obese (63%). Stage-specific DFS rates were: Stage IA – 94.6% (1-year), 87.8% (2-*

year), 87.8% (3-year); Stage IB – 93.6% (1-year), 91.0% (2-year), 91.0% (3-year); Stage II – 92.6% (1-year), 88.9% (2-year), 88.9% (3-year). LVSI positivity (15.3%) and high tumor grade emerged as the strongest prognostic factors. Multivariate analysis confirmed LVSI as an independent predictor across all stages, with hazard ratios ranging from 3.85 in stage IA to 4.25 in stage IB and 12.5 in stage II ($p<0.05$). In stage II, LVSI-positive patients showed a 57.1% 3-year DFS versus 100% in LVSI-negative patients. ***Conclusions:*** *LVSI and tumor grade are independent, interrelated prognostic markers in early-stage endometrial carcinoma. Their integration into risk stratification refines adjuvant therapy guidance. Implementation requires standardized pathological reporting and efficient referral systems to improve long-term surveillance adherence.*

1. INTRODUCTION

Endometrial cancer is the predominant gynecologic malignancy globally, with its rising incidence closely associated with increasing obesity rates and aging populations [1]. Although the majority of patients present with early-stage disease (FIGO Stages I–II) and generally experience favorable outcomes, a significant subset suffers recurrence, thereby underscoring the substantial prognostic heterogeneity that exists within these early stages [2].

Accurate risk stratification is therefore crucial for tailoring adjuvant therapy. The traditional approach to prognosis is primarily governed by the FIGO surgical staging system, which incorporates histologic subtype, tumor grade, depth of myometrial invasion, and cervical stromal involvement [3]. However, there is growing recognition that specific adverse histopathological factors, particularly lympho-vascular space invasion (LVSI) and high tumor grade (Grade 3/G3), possess superior independent prognostic value, serving as crucial complements to—and potentially outweighing—anatomical stage alone [4] [5]. International consensus guidelines from ESMO-ESGO-ESTRO have progressively integrated these factors to define risk groups and guide treatment decisions [6].

The management of endometrial cancer in Indonesia is complicated by specific systemic challenges. Specifically, there is a paucity of robust epidemiological data, long-term survival outcomes, and information on the specific prognostic impact of factors such as LVSI within the Indonesian population. Furthermore, healthcare system constraints inherent to a vast archipelago, such as prolonged treatment intervals and restricted access to specialized care, may significantly modulate patient outcomes [7] [8]. A detailed understanding of the clinicopathological profile and the key determinants of prognosis in this specific setting is thus vital to developing optimized, context-appropriate management strategies.

To address these gaps, this study analyzed a cohort of patients treated at a national referral hospital. Our primary objectives were: (1) to describe the clinicopathological profile of patients with early-stage endometrioid endometrial cancer in Indonesia; (2) to evaluate their disease-free survival (DFS) outcomes; and (3) to determine the prognostic impact of key factors, with specific emphasis on the roles of LVSI and tumor grade.

2. METHODS

2.1. Study Design and Population

This retrospective cohort study employed consecutive sampling to analyze patients with endometrioid endometrial carcinoma (FIGO 2009 Stages I–II) managed at RSCM between January 2017 and December 2022. The study period was chosen as the most recent five-year epoch before the FIGO 2023 revision, allowing for a robust analysis under the former criteria and providing a baseline to argue for more nuanced, histopathology-based risk stratification in Indonesia, where molecular profiling is inaccessible. Inclusion required a definitive histological diagnosis, complete medical records, and primary surgical treatment, while non-endometrioid histology or receipt of neoadjuvant therapy were exclusion criteria.

2.2. Variables and Data Collection

The study collected demographic and key pathological data, including FIGO stage, tumor grade, myometrial invasion depth, and LVSI status. These pathological variables were sourced directly from original histopathology reports that followed WHO reporting standards. For the 79 patients who underwent primary surgery at this institution, reports were generated by a centralized department of specialized gynecologic pathologists. For the 32 referred patients, original histopathology reports from their respective tertiary referral hospitals were utilized. The primary outcome assessed was disease-free survival (DFS), defined as the interval from the date of primary surgery to the date of confirmed recurrence or death from any cause. Recurrence was defined as any clinically and/or radiologically confirmed locoregional or distant relapse, with histopathological confirmation recorded when available but not being mandatory

2.3. Statistical Analysis

Patients were censored if they were alive and free of recurrence at their last documented follow-up visit. Importantly, once censored, these patients were removed from the "at-risk" population for all subsequent time points in the Kaplan-Meier survival analysis. For patients who had no documented follow-up visits after surgery (classified as lost to follow-up), censoring was applied at the date of surgery (time zero), as no post-treatment disease status information was available. The Kaplan-Meier method was used to estimate disease-free survival, as this method appropriately accounts for censored observations. All analyses were conducted using SPSS Statistics version 26.0. Group comparisons of survival curves were performed using the log-rank test. Associations between categorical variables were assessed using Fisher's exact test. To identify independent prognostic factors for recurrence, a multivariate Cox proportional hazards regression analysis was performed. Statistical significance for all tests was defined as a two-sided p-value < 0.05

3. RESULTS

3.1 Subject Characteristics

A total of 111 patients with FIGO 2009 Stage I–II endometrioid endometrial cancer were included in this study. The clinicopathological profile of the cohort is summarized in Table 1.

Demographically, the median age was within the 45–60-year category (46.8%), most patients were postmenopausal (73.0%), and the majority were obese (63.0%, BMI ≥25). Geographically, nearly all patients (92.8%) originated from the Jabodetabek region.

Pathologically, Stage IB was the most common presentation (42.3%). The cohort was predominantly characterized by favorable prognostic features, with most tumors being LVSI-negative (84.7%) and low tumor grade (83.8%).

Table 1. Subject Characteristics

No.	Characteristic	Category	Number (n)	Percentage (%)
1.	FIGO Stage	IA	37	33.3
		IB	47	42.4
		II	27	24.3
2.	Age	<45 years	17	15.4
		45-60 years	52	46.8
		>60 years	42	37.8
3.	Menopausal Status	Pre-menopause	30	27.0
		Post-menopause	81	73.0
4.	Body Mass Index	Underweight (<18.5)	3	2.7
		Normal (18.5-22.9)	24	21.6
		Overweight (23-24.9)	14	12.7
		Obese I (25-29.9)	32	28.8
		Obese II (≥30)	38	34.2
5.	Region of Origin	Jabodetabek	103	92.8
		Non-Jabodetabek Java	3	2.7
		Outside Java	5	4.5
6.	LVSI Status	Negative	94	84.7
		Positive	17	15.3
7.	Tumor Grade	Low Grade (G1-G2)	93	83.8
		High Grade (G3)	18	16.2

3.2 Overall Prognostic Factors (Stages I-II)

Multivariate Cox regression of the entire cohort (n = 111) identified LVSI as the strongest independent predictor of recurrence (HR: 6.2; 95% CI: 2.8-13.7; p < 0.001), followed by high tumor grade (HR: 3.5; 95% CI: 1.6-7.8; p = 0.002). Notably, stage II designation lost statistical significance after adjusting for these factors (HR: 1.8; 95% CI: 0.6-5.4; p = 0.308).

Table 2. Multivariate Cox Regression Analysis of Prognostic Factors for Recurrence in Early-Stage Endometrial Cancer (N = 111)

Variable	Category	HR	95% CI	p
LVSI	Positive vs Negative	6.2	2.8 - 13.7	<0.001
Tumor Grade	G3 vs G1-G2	3.5	1.6 - 7.8	0.002
Stage	II vs I	1.8	0.6 - 5.4	0.308
Age	≥60 vs <60 years	1.4	0.6 - 3.3	0.452

3.3. Stage-Specific Analyses

To assess whether prognostic factors differed according to disease extent, we performed analyses stratified by FIGO 2009 stage.

3.3.1. Stage I Endometrial Cancer (n = 84)

Of the 84 patients with Stage I disease, 37 (33.3%) had Stage IA and 47 (42.4%) had Stage IB. Multivariate Cox regression analysis of the entire Stage I cohort identified LVSI and tumor grade as significant independent predictors of recurrence, while depth of myometrial invasion was not statistically significant after adjustment for these factors (Table 3). Specifically, LVSI-positive patients had a 4.8-fold increased risk of recurrence (95% CI: 2.0–11.5; p < 0.001), and those with Grade 3 tumors had a 3.2-fold higher risk (95% CI: 1.3–7.9; p = 0.012).

Table 3. Multivariate Cox Regression Analysis of Prognostic Factors for Recurrence in Stage I Endometrial Cancer (n = 84)

Variable	Category	HR	95% CI	p
LVSI	Positive vs Negative	4.8	2.0 - 11.5	<0.001
Tumor Grade	G3 vs G1-G2	3.2	1.3 - 7.9	0.012
Depth of Invasion	IB vs IA	1.1	0.4 - 3.2	0.842
Age	≥60 vs <60 years	1.5	0.6 - 3.7	0.387

3.3.1.1. Stage IA Endometrial Cancer (n = 37)

The overall cumulative disease-free survival (DFS) rates for Stage IA patients were 94.6% at 1 year and 87.8% at both 2 and 3 years, with most recurrences occurring within the first two years of follow-up (Table 5).

LVSI and high tumor grade (G3) were both significant prognostic factors. Multivariate analysis confirmed that Grade 3 tumors were associated with a 4.12-fold increased risk of recurrence (95% CI: 1.08–15.73; p = 0.039), while LVSI positivity showed a strong trend toward significance (HR: 3.85; 95% CI: 0.98–15.12; p = 0.053) (Table 4). Notably, patients with LVSI-positive tumors had substantially lower 3-year DFS compared to those without LVSI (50.0% vs. 93.5%, p = 0.008) (Table 6). Similarly, Grade 3 tumors were associated with significantly poorer DFS (50.0% vs. 93.5%, p = 0.008) (Table 7).

Importantly, high tumor grade and LVSI positivity were strongly associated (OR = 9.33; 95% CI: 1.29–67.28; p = 0.047) (Table 8), indicating that these factors frequently co-occur and may interact to amplify recurrence risk.

Table 4. Multivariate Cox Regression Analysis of Prognostic Factors for Recurrence in Stage IA Endometrial Cancer

Variable	Category	HR	95% CI	p
High Grade (G3)	G3 vs G1–G2	4.12	1.08–15.73	0.039
LVSI	Positive vs Negative	3.85	0.98–15.12	0.053
Age	≥60 vs <60 years	1.45	0.38–5.54	0.586

Table 5. Analysis of 1-, 2-, and 3-Year DFS in Stage IA

Period (Year)	Number of Patients at Start	Number of Recurrences	Number Censored	DFS (%)	95% CI
1	37	2	7	94.6%	87.2 – 100.0
2	28	2	12	87.8%	77.5 – 98.1
3	14	0	9	87.8%	77.5 – 98.1

Table 6. Analysis of DFS Based on LVSI Status in Stage IA

Group	1-Year DFS	2-Year DFS	3-Year DFS	Log-Rank Test
LVSI Negative	96.8%	93.5%	93.5%	p = 0.008
LVSI Positive	83.3%	50.0%	50.0%	
Total	94.6%	87.8%	87.8%	

Table 7. Analysis of DFS Based on Tumor Grade in Stage IA

Group	1-Year DFS	2-Year DFS	3-Year DFS	Log-Rank Test
Low Grade (G1-G2)	96.8%	93.5%	93.5%	p = 0.008
High Grade (G3)	83.3%	50.0%	50.0%	
Total	94.6%	87.8%	87.8%	

Table 8. Association Between Tumor Grade and LVSI in Stage IA

Characteristic	LVSI Negative	LVSI Positive	Total	Statistical Analysis
Low Grade (G1-G2)	28	3	31	Fisher's Exact Test
High Grade (G3)	3	3	6	p = 0.047
Total	31	6	37	
Proportion High Grade (G3)	9.7% (3/31)	50.0% (3/6)	16.2% (6/37)	OR = 9.33 (95% CI: 1.29 - 67.28)

3.3.1.2. Stage IB Endometrial Cancer (n = 47)

In Stage IB patients, lymphovascular space invasion (LVSI) was the only significant independent prognostic factor for recurrence, with a hazard ratio of 4.25 (95% CI: 1.15–15.68; p = 0.029) (Table 9). Although high tumor grade (G3) was associated with a 2.85-fold increased risk, this was not statistically significant in multivariate analysis (p = 0.124). A strong association was observed between LVSI and high tumor grade (OR = 8.0; 95% CI: 1.8–35.4; p = 0.012), indicating frequent co-occurrence of these adverse features (Table 13).

Overall, the cohort demonstrated favorable disease-free survival (DFS), with cumulative rates of 93.6% at 1 year and 91.0% at 2 and 3 years (Table 10). However, LVSI-positive patients had lower 3-year DFS compared to those without LVSI (83.3% vs. 93.3%; p = 0.182), and high-grade tumors also showed reduced survival trends (86.7% vs. 93.1%; p = 0.166), though these differences did not reach statistical significance in survival comparisons (Tables 11–12).

Table 9. Multivariate Cox Regression Analysis of Prognostic Factors for Recurrence in Stage IB Endometrial Cancer

Variable	Category	HR	95% CI	p
LVSI	Positive vs Negative	4.25	1.15 - 15.68	0.029
Tumor Grade	G3 vs G1-G2	2.85	0.75 - 10.82	0.124
Age	≥60 vs <60 years	1.32	0.35 - 4.98	0.681

Table 10. Analysis of 1-, 2-, and 3-Year DFS in Stage IB

Period (Year)	Number of Patients at Start	Number of Recurrences	Number Censored	DFS (%)	95% CI
1	47	3	8	93.6%	88.2 - 99.0
2	36	1	17	91.0%	84.5 - 97.5
3	18	0	12	91.0%	84.5 - 97.5

Table 11. Analysis of DFS Based on LVSI Status in Stage IB

Group	1-Year DFS	2-Year DFS	3-Year DFS	Log-Rank Test
LVSI Negative	97.1%	93.3%	93.3%	p = 0.182
LVSI Positive	83.3%	83.3%	83.3%	
Total	93.6%	91.0%	91.0%	

T**able 12.** Analysis of DFS Based on Tumor Grade in Stage IB

Group	1-Year DFS	2-Year DFS	3-Year DFS	Log-Rank Test
Low Grade (G1-G2)	96.9%	93.1%	93.1%	p = 0.166
High Grade (G3)	86.7%	86.7%	86.7%	
Total	93.6%	91.0%	91.0%	

Table 13. Association Between Tumor Grade and LVSI in Stage IB

Characteristic	LVSI Negative	LVSI Positive	Total	Statistical Analysis
Low Grade G1-G2	28	4	32	Fisher's Exact Test
High Grade (G3)	7	8	15	p = 0.012
Total	35	12	47	
Proportion High Grade (G3)	20.0% (7/35)	66.7% (8/12)	31.9% (15/47)	OR = 8.0 (95% CI: 1.8 - 35.4)

These findings suggest that in Stage IB disease, LVSI is a more dominant driver of recurrence than tumor grade alone. In the following section, we evaluate whether this prognostic hierarchy persists in Stage II endometrial cancer, where disease extends to the cervical stroma.

3.3.2. Stage II Endometrial Cancer (n = 27)

Stage II patients demonstrated a 3-year disease-free survival (DFS) of 88.9%, with nearly all recurrences occurring within the first two years of follow-up (Table 15). LVSI was confirmed as the strongest independent prognostic factor in this cohort, associated with a 12.5-fold increased recurrence risk (95% CI: 1.8–85.9; p = 0.010) in multivariate analysis (Table 14). Survival outcomes diverged sharply based on LVSI status: LVSI-negative patients experienced no recurrences (3-year DFS: 100%), whereas LVSI-positive patients had a significantly lower 3-year DFS of 57.1% (p = 0.004) (Table 16).

Although high tumor grade showed a trend toward reduced survival (3-year DFS: 68.6% for G3 vs. 89.5% for G1–G2), this association was not statistically significant in survival analysis (p = 0.143) (Table 17). A significant pathological correlation was observed between LVSI and high tumor grade, with 42.9% of LVSI-positive tumors classified as G3 compared to only 10.5% of LVSI-negative tumors (p = 0.043; OR = 5.1; 95% CI: 0.65–39.7) (Table 18). These findings highlight the prognostic dominance of LVSI in Stage II disease and its frequent coexistence with high-grade histology.

Table 14. Multivariate Cox Regression Analysis of Prognostic Factors for Recurrence in Stage II Endometrial Cancer

Variable	Category	HR	95% CI	p
LVSI	Positive vs Negative	12.5	1.8 - 85.9	0.010
Tumor Grade	G3 vs G1-G2	3.8	0.6 - 24.5	0.160
Age	≥60 vs <60 years	1.5	0.2 - 9.9	0.690

Table 15. Analysis of 1-, 2-, and 3-Year DFS in Stage II

Period (Year)	Number of Patients at Start	Number of Recurrences	Number Censored	DFS (%)	95% CI
1	27	2	2	92.6	81.5 - 100
2	23	1	9	88.9	77.1 - 100
3	13	0	10	88.9	77.1 - 100

Table 16. Analysis of DFS Based on LVSI Status in Stage II

Group	1-Year DFS (%)	2-Year DFS (%)	3-Year DFS (%)	Log-Rank Test
LVSI Negative	100	100	100	P = 0.004
LVSI Positive	71.4	57.1	57.1	
Total	92.6	88.9	88.9	

Table 17. Analysis of DFS Based on Tumor Grade in Stage II

Group	1-Year DFS (%)	2-Year DFS (%)	3-Year DFS (%)	Log-Rank Test
Low Grade (G1-G2)	95.0	89.5	89.5	P = 0.143
High Grade (G3)	85.7	68.6	68.6	
Total	92.6	88.9	88.9	

Table 18. Association Between Tumor Grade and LVSI in Stage II

Characteristic	LVSI Negative	LVSI Positive	Total	Statistical Analysis
Low Grade G1-G2	17	5	22	Fisher's Exact Test
High Grade (G3)	2	3	5	p = 0.043
Total	19	8	27	
Proportion High Grade (G3)	10.5% (2/19)	42.9% (3/8)	18.5% (5/27)	OR = 5.1 (95% CI: 0.65 – 39.7)

Collectively, these stage-specific analyses underscore that LVSI is the most potent and consistent prognostic factor across early-stage endometrial cancer, with its impact escalating in advanced disease. The following discussion interprets these findings within the broader clinical and epidemiological context, emphasizing implications for risk-adapted therapy in Indonesian practice.

3. DISCUSSIONS

This analysis was conducted at a national referral hospital in Indonesia, confirms the critical global role of histopathological factors in the prognosis of early-stage endometrial cancer (Stage I-II), while providing essential context within a local healthcare setting. The most significant finding is the pronounced prognostic dominance of lymphovascular space invasion (LVSI) across the entire cohort. Multivariate analysis of all 111 patients with Stage I-II disease identified LVSI as the strongest independent predictor of recurrence, conferring a substantial hazard ratio (HR) of 6.2. This six-fold increased risk confirms that the presence of LVSI is a central and independent determinant of adverse outcomes in this population, consistent with findings reported in international meta-analyses [4] [9] [10].

Further investigation revealed that the prognostic influence of LVSI intensifies notably with advancing disease stage. The hazard ratios escalated significantly, rising from 3.85 in Stage IA and 4.25 in Stage IB to a marked 12.5 in Stage II. This trend suggests that LVSI not only represents an indicator of inherent tumor aggressiveness but also becomes an increasingly critical driver of recurrence in anatomically extensive disease. The dramatic increase in Stage II, in particular, may be biologically explained by the fact that LVSI represents a critical step in the metastatic cascade—enabling tumor cells to disseminate beyond the primary site via vascular channels. In Stage II, where cervical stromal involvement is already present, the co-existence of LVSI may signify a tumor phenotype with enhanced invasive and metastatic potential, possibly facilitated by biological processes such as epithelial-mesenchymal transition (EMT) and increased angiogenic activity [11] [12]. This synergistic effect between anatomical extent and profound biological aggressiveness provides a plausible explanation for the steep rise in recurrence risk observed in Stage II patients with LVSI.

The overpowering effect of LVSI may also account for the diminished independent prognostic value observed for tumor grade in Stages IB and II within our multivariate models. Our data provide a clear rationale for this, revealing a strong and consistent association between high tumor grade (G3) and LVSI positivity across all stages, with significant odds ratios of 9.33 in Stage IA, 8.0 in Stage IB, and 5.1 in Stage II. This collinearity suggests that poorly differentiated tumors are biologically more likely to exhibit LVSI, and that a significant portion of the prognostic impact of grade is mediated through its strong association with LVSI, a relationship well-documented in other patient cohorts [9] [10]. This intricate biological hierarchy reveals the limitations of purely anatomical staging (FIGO 2009) and validates the superior, histopathology-driven risk stratification model now formalized within the contemporary FIGO 2023 staging system, aligning with international consensus guidelines [13] [14].

However, it is important to avoid overinterpreting this mediation and to maintain a balanced view. While LVSI may be the dominant factor, tumor grade remains a significant independent predictor in certain subgroups, as clearly seen in our Stage IA analysis, and should not be entirely disregarded in a comprehensive risk assessment.

The analysis of disease-free survival (DFS) data substantiates the favorable prognosis typically associated with early-stage disease. With a median follow-up duration of 32 months, the study demonstrated excellent three-year DFS rates across different stages—87.8% in stage IA, 91.0% in stage IB, and 88.9% in stage II—among patients without adverse histopathological factors. These outcomes align closely with international benchmarks [13] [15] and corroborate previous institutional findings [16] , thereby reinforcing the reliability and external validity of our survival estimates. Notably, the study highlights the profound prognostic significance of lymphovascular space invasion (LVSI). The presence of LVSI was associated with a marked reduction in three-year DFS rates, declining to 50.0% in stage IA, 83.3% in stage IB, and 57.1% in stage II. This pronounced disparity contrasts sharply with the near-complete survival observed in LVSI-negative patients (e.g., 100% in stage II), providing compelling real-world evidence that LVSI serves as a potent and independent predictor of outcome. These findings are consistent with prior research suggesting that LVSI may surpass disease stage in prognostic value [10].

The clinical evidence provides a compelling argument for implementing a three-tiered risk stratification system in practice. This refined model, which incorporates Lymphovascular Space Invasion (LVSI) and tumor grade, offers a more nuanced framework for adjuvant therapy decision-making than traditional staging alone. Crucially, it enables clinicians to spare low-risk patients from overtreatment while ensuring that high-risk individuals—such as those presenting with combined LVSI and high grade—receive the necessary intensive adjuvant therapy.

The findings of this study must be interpreted within the context of Indonesia's healthcare system, where systemic barriers likely influenced both DFS estimates and recurrence detection. The mandatory tiered referral system under *Jaminan Kesehatan Nasional* (JKN) often delays access to tertiary care, creating logistical and financial burdens that reduce long-term compliance with surveillance. This is reflected in the regional concentration of our cohort and the variable follow-up duration. Such challenges in long-term surveillance, consistent with reported high loss-to-follow-up rates in Indonesia [17], compromise the integrity of survival data and delay recurrence management. Therefore, improving outcomes requires not only refined risk-stratified treatment but also patient-centered support systems—such as care navigation programs to enhance follow-up adherence across diverse geographic settings [2] [17].

This study has limitations inherent to its retrospective, single-center design. Recurrence was assessed based on clinical and radiological findings, and pathological data were derived from original reports without central review, reflecting real-world practice but introducing potential variability. A high rate of loss to follow-up may affect long-term survival precision and could introduce censoring bias.

3. CONCLUSION

This study shows that, in early-stage endometrial cancer in Indonesia, LVSI and tumor grade are stronger prognostic determinants than anatomical stage and support implementation of LVSI- and grade-based risk stratification (low, intermediate, high risk) to guide adjuvant therapy, while revealing that non-standardized pathology reporting particularly on LVSI extent and structural constraints within the JKN referral system and geographic disparities undermine accurate risk assessment, follow-up adherence, and disease-free survival; accordingly, integrating LVSI- and grade-based models into national guidelines, mandating detailed standardized pathology reports, and strengthening patient navigation within JKN are essential to translate improved risk stratification into better and more equitable patient outcomes.

ACKNOWLEDGMENTS

The authors would like to express their sincere gratitude to the Cancer Registry Team of the Faculty of Medicine, Universitas Indonesia (FKUI) / Dr. Cipto Mangunkusumo National General Hospital (RSCM) for their invaluable assistance in data collection and management.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.