Submitted: 17 September, 2024 Accepted: 22 October, 2024 Published: 15 February, 2025 DOI:10.22514/ejgo.2025.024

ORIGINAL RESEARCH

European Journal of Gynaecological Oncology

Isolated lymph node recurrence and prognosis in endometrioid type endometrial cancer

Varol Gülseren[1,*], İlker Çakır[2], İsa Aykut Özdemir[3], Kemal Güngördük[4]

[1]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, School of Medicine, Erciyes University, 38039 Kayseri, Turkey
[2]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Tepecik Education and Research Hospital, 35020 İzmir, Turkey
[3]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, School of Medicine, Medipol University, 34214 İstanbul, Turkey
[4]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, School of Medicine, Muğla Sıtkı Koçman University, 48000 Muğla, Turkey

***Correspondence**
varol.gul@erciyes.edu.tr
(Varol Gülseren)

Abstract

Background: We compared treatment strategies for recurrence in patients who underwent surgery for endometrioid-type endometrial cancer (EC) and developed isolated retroperitoneal lymph node recurrence (ILNR) during follow-up. Additionally, we evaluated prognostic factors affecting post-recurrence survival (PRS). **Methods**: This retrospective study included patients treated with at least a hysterectomy and oophorectomy for endometrioid-type EC at our clinic between 2004 and 2023. **Results**: Among the 24 patients who developed ILNR after surgery for endometrioid-type EC, 6 (25.0%) had metastasis confined to the pelvic lymph nodes (PLNs), 7 (29.2%) to the para-aortic lymph nodes (PaLNs) and 11 (45.8%) to both PLNs and PaLNs. PRS $\geq$24 months was observed in 8 (33.3%) patients. Cox regression analysis was performed to identify significant prognostic factors associated with long-term PRS. In the univariate analysis, grade 3 tumors at initial surgery, disease-free survival (DFS) $\geq$18 months and surgical resection during recurrence were identified as significant prognostic factors. However, multivariate analysis did not reveal any independent prognostic factors. **Conclusions**: Although no independent prognostic factors for long-term PRS were identified in patients with ILNR after surgery for endometrioid-type EC, grade 3 tumors at initial surgery are possibly associated with worse outcomes. Prolonged DFS (>18 months) and surgical resection are possible predictors of better outcomes.

Keywords

Endometrial cancer; Lymph node; Recurrence; Surgery

1. Introduction

Endometrial cancer (EC) is the most common gynecological malignancy and the fourth most common cancer among adult women in developed countries [1]. Despite a generally favorable prognosis, the recurrence rate of EC ranges from 10% to 23% [2, 3]. The prognosis and management of metastasis are strongly influenced by the site of recurrence, number of recurrences and initial treatment. Lymph node (LN) recurrence occurs in 4–20% of early-stage EC cases and in approximately 8–50% of advanced-stage cases [4, 5]. The risk of recurrence and lymphatic spread is particularly high in serous and clear cell tumors.

At the time of diagnosis, approximately 8% of patients present with retroperitoneal pelvic LN (PLN) and/or para-aortic LN (PaLN) metastases [6]. Retroperitoneal PLN and PaLN dissection is associated with complications such as lymphedema, lymphocyst formation and intraoperative vascular injury. Recently, the introduction of sentinel LN biopsy combined with ultrastaging has facilitated highly accurate staging with low morbidity. However, a major concern with sentinel LN mapping is the risk of isolated LN recurrence, particularly when complete lymphadenectomy has not been performed. Isolated retroperitoneal LN recurrence (ILNR) in patients with EC is rare, and the prognostic factors and treatment strategies associated with improved overall survival (OS) remain poorly understood.

The aim of this study was to compare treatment strategies for recurrence in patients who underwent surgery for endometrioid-type EC and subsequently developed ILNR during follow-up, as well as to evaluate significant prognostic factors influencing survival after recurrence.

2. Methods

This retrospective study included patients who underwent hysterectomy and oophorectomy for endometrioid-type EC at our clinic between 2004 and 2023. The inclusion criteria for the study were patients with endometrioid type endometrial tumors, patients without any other accompanying cancer and patients with only retroperitoneal lymph node recurrence during follow-up after hysterectomy. Exclusion criteria were patients with non-endometrioid type tumors, having accompanying cancer, having multiple organ metastases and inability to undergo surgery at initial diagnosis due to medical reasons. Retroperitoneal (PLN and/or PaLN) LN dissection and omen-

tectomy were documented based on surgical and pathology reports. Patients who were inoperable for medical reasons, as well as those who underwent fertility preservation procedures and did not complete follow-up at our center, were excluded from the study. This study was approved by the Tepecik Research and Treatment Hospital Local Ethics Committee (Decision number: 2021/01-30). As this study involved a retrospective review of a database, subjects' consent to participate was not deemed necessary. All procedures adhered to the ethical standards of the institutional and/or national research committees, the 1964 Declaration of Helsinki, and its subsequent amendments or comparable ethical guidelines.

All surgeries were performed by experienced gynecologic oncologists. The diagnosis of EC was confirmed through preoperative biopsies. During the initial operation, the following areas were thoroughly examined: intestinal mesentery, serosa, liver capsule, stomach, paracolic regions, Douglas peritoneum, omentum and subdiaphragmatic peritoneum. Patients underwent hysterectomy and bilateral oophorectomy. An extrafascial hysterectomy (type 1) involved complete removal of the uterus and cervix without excision of parametrial or paravaginal tissues. The management of EC varied, particularly with respect to LN evaluation. The extent of LN dissection—whether only PLN dissection, PLN and PaLN dissection, or sentinel LN biopsy—was documented. Pathological assessments were conducted by gynecologic pathologists, and the number of harvested LNs was recorded. PLN dissection involved the removal of lymphatic tissue overlying the external and common iliac vessels, as well as tissue within the obturator fossa. Para-aortic LN dissection extended from the bifurcation of the inferior vena cava and aorta down to the area below the left renal vein. If no bulky LNs were detected, LNs distal to the deep circumflex external iliac vein and below the obturator nerve were not removed.

The surgical procedures, adjuvant treatments and survival statuses of the patients were determined from their medical records. Lymphovascular space invasion, tumor size, depth of myometrial invasion, cervical involvement, adnexal involvement and LN status were obtained from pathology reports. Patients with stage I–II disease were categorized as early stage, whereas those with stage III–IV disease were categorized as advanced stage. The diagnosis of LN metastasis in surgically treated patients was based on pathology examinations, whereas in patients treated with chemotherapy or radiotherapy, it was determined based on imaging findings. Patients with ILNR were categorized according to the location of metastases: only PLNs, only PaLNs or both PLNs and PaLNs (PPaLNs). Distant organ metastasis was assessed using computed tomography, magnetic resonance imaging or positron emission tomography-computed tomography. Although some patients presented with symptoms, many ILNR cases were identified during routine follow-up. All patients were followed every 3 months for the first 2 years, every 6 months for the next 3 years and annually thereafter. Follow-up evaluations included vaginal speculum examinations and pelvic ultrasonography. Annual cytological assessments were performed using vaginal smears, and computed tomography or magnetic resonance imaging was conducted annually. Patients with suspicious findings underwent positron emission tomography-computed tomography. Imaging findings were compared with previous evaluations.

ILNR was defined as the occurrence of LN metastasis confined to the retroperitoneal space, without metastasis to solid organs or the peritoneum, during follow-up in patients who underwent surgery for EC. Disease-free survival (DFS) was defined as the time between the date of primary surgery and the detection of recurrence or the final observation. OS was defined as the time between the date of primary surgery and death or the final observation. Post-recurrence survival (PRS) was defined as the time between recurrence and death or the final follow-up. PRS $<$24 months was categorized as short-term PRS, whereas PRS $\geq$24 months was categorized as long-term PRS.

Numerical values were compared using Student's *t*-test and are presented as means $\pm$ standard deviations. Categorical variables are presented as frequencies and percentages. The chi-squared test was used to analyze categorical data; the Pearson chi-squared test was applied when fewer than 20% of the groups contained fewer than five patients. If more than 20% of the groups had fewer than five patients and the minimum expected count was below five, Fisher's exact test was used. The optimal cut-off values for prognostic factors associated with long-term PRS were identified using receiver operating characteristic analysis, and areas under the curve (AUC) were calculated. Cox regression analysis was performed to identify predictive factors, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Survival analysis was conducted using the Kaplan-Meier method; comparisons were made via the log-rank test. Data were analyzed using SPSS software (version 17; IBM Corp., Armonk, NY, USA). *p*-values < 0.05 were considered statistically significant.

3. Results

Among the 24 patients who underwent surgery for endometrioid-type EC and developed ILNR during follow-up, 6 (25.0%) had metastasis confined to the PLNs, 7 (29.2%) had metastasis solely in the PaLNs and 11 (45.8%) had metastasis in both PPaLNs. Table 1 presents the patients' clinical and demographic characteristics. The mean age was 63.3 $\pm$ 8.7 years, and the mean tumor size was 4.4 $\pm$ 2.3 cm. Grade 3 tumors were the most frequently observed, affecting 13 patients (54.2%). Lymphovascular space invasion was found in 18 patients (75.0%); there were no significant differences among metastasis locations (83.3% for PLN recurrence, 85.7% for PaLN recurrence and 63.6% for PPaLN recurrence; $p = 0.495$).

During the initial surgery, LN dissection was not performed in one patient (4.2%), sentinel LN biopsy was conducted in two patients (8.3%), PLN dissection alone was performed in four patients (16.7%) and PPaLN dissection was completed in 17 patients (70.8%). With regard to initial staging, seven patients (29.2%) were categorized as stage I–II, whereas 17 (70.8%) were categorized as stage III–IV; there were no significant differences based on metastasis localization ($p = 0.133$). The most common adjuvant treatment after initial surgery was chemotherapy combined with external beam radiotherapy (EBRT), administered to 12 patients (50.0%). The mean time

TABLE 1. Patient clinical and demographic characteristics.

	PLN n = 6 (25.0%)	PaLN n = 7 (29.2%)	PPaLN n = 11 (45.8%)	*p*	Total n = 24 (100.0%)
Age at initial diagnosis, yr	64.8 ± 10.7	64.4 ± 12.2	61.9 ± 4.9	0.766	63.3 ± 8.7
Tumor size, cm	4.3 ± 2.4	4.9 ± 1.2	4.2 ± 2.8	0.831	4.4 ± 2.3
High CA125 (>35 U/mL)	3 (50.0%)	3 (42.9%)	3 (27.3%)	0.614	9 (37.5%)
Grade					
- 1	2 (33.3%)	-	3 (27.3%)		5 (20.8%)
- 2	2 (33.3%)	2 (28.6%)	2 (18.2%)	0.493	6 (25.0%)
- 3	2 (33.3%)	5 (71.4%)	6 (54.5%)		13 (54.2%)
LVSI	5 (83.3%)	6 (85.7%)	7 (63.6%)	0.495	18 (75.0%)
Deep myometrial invasion	3 (50.0%)	6 (85.7%)	4 (36.4%)	0.313	13 (54.2%)
Lymphadenectomy					
- None	-	-	1 (9.1%)		1 (4.2%)
- Sentinel only	2 (33.3%)	-	-	0.117	2 (8.3%)
- Pelvic only	2 (33.3%)	1 (14.3%)	1 (9.1%)		4 (16.7%)
- PPaLNs	2 (33.3%)	6 (85.7%)	9 (81.8%)		17 (70.8%)
LN involvement					
- Pelvic LNs	1 (16.7%)	4 (57.1%)	8 (72.7%)	0.084	13 (54.2%)
- Paraaortic LNs	-	1 (14.3%)	5 (45.5%)	0.087	6 (25.0%)
Stage					
- I–II	3 (50.0%)	3 (42.9%)	1 (9.1%)	0.133	7 (29.2%)
- III–IV	3 (50.0%)	4 (57.1%)	10 (90.9%)		17 (70.8%)
Adjuvant therapy					
- Observation ± VBT	4 (66.7%)	1 (14.3%)	-		5 (20.8%)
- EBRT ± VBT	-	1 (14.3%)	2 (18.2%)	0.015	3 (12.5%)
- Chemotherapy ± VBT	2 (33.3%)	-	2 (18.2%)		4 (16.7%)
- Chemotherapy + EBRT	-	5 (71.4%)	7 (63.6%)		12 (50.0%)
Time to recurrence after initial diagnosis	20.5 ± 12.4	16.2 ± 6.5	17.6 ± 8.4	0.704	17.9 ± 8.8
ILNR treatment					
- CT only	-	4 (57.1%)	4 (36.4%)		8 (33.3%)
- RT only	3 (50.0%)	1 (14.3%)	1 (9.1%)	0.070	5 (20.8%)
- Resection + CT or RT	2 (33.3%)	2 (28.6%)	1 (9.1%)		5 (20.8%)
- RT + CT	1 (16.7%)	-	5 (45.5%)		6 (25.0%)

LN: lymph node; PLN: pelvic lymph node; PaLN: paraaortic lymph node; LVSI: lymphovascular space invasion; VBT: vaginal brachytherapy; EBRT: external beam radiotherapy; ILNR: isolated lymph node recurrence; RT: radiotherapy; CT: chemotherapy; CA125: Cancer Antigen 125; PPaLNs: Pelvic and Paraaortic Lymph node.

to ILNR development was 17.9 ± 8.8 months.

Concerning recurrence treatment, three patients (50.0%) with PLN recurrence received radiotherapy alone, two (33.3%) underwent surgery combined with chemotherapy or radiotherapy and one (16.7%) received a combination of chemotherapy and radiotherapy. Among patients with PaLN recurrence, the most common treatment was chemotherapy alone, administered to four patients (57.1%). In the group with PPaLN recurrence, five patients (45.5%) received a combination of radiotherapy and chemotherapy, whereas four (36.4%) received chemotherapy alone. No significant differences in recurrence treatment were observed based on metastasis location (p = 0.070).

In total, 16 patients (66.7%) had PRS <24 months, and 8 (33.3%) had PRS ≥24 months. Table 2 presents the clinical characteristics of the short-term and long-term PRS groups. Although not statistically significant, a higher proportion of grade 3 tumors was observed in the short-term PRS group (68.8% *vs.* 25.0%; p = 0.083). Deep myometrial invasion during initial surgery was observed in 11 patients (68.8%) in the short-term PRS group and two patients (25.0%) in the long-term PRS group (p = 0.154). Furthermore, at the time of initial diagnosis, 11 patients (68.8%) in the short-term PRS group and six patients (75.0%) in the long-term PRS group

TABLE 2. Clinical characteristics of patients with short- and long-term post-recurrence survival.

	Short-term PRS n = 16 (66.7%)	Long-term PRS n = 8 (33.3%)	*p*
Age at initial diagnosis, yr	63.3 ± 10.0	63.3 ± 5.8	1.000
Tumor size, cm	4.9 ± 2.5	3.4 ± 1.4	0.134
High CA125 (>35 U/mL)	7 (43.8%)	2 (25.0%)	0.332
Grade			
- 1	3 (18.8%)	2 (25.0%)	
- 2	2 (12.5%)	4 (50.0%)	0.083
- 3	11 (68.8%)	2 (25.0%)	
Lymphovascular space invasion	13 (81.3%)	5 (62.5%)	0.302
Deep myometrial invasion	11 (68.8%)	2 (25.0%)	0.154
Lymphadenectomy			
- None	1 (6.3%)	-	
- Sentinel only	2 (12.5%)	-	0.553
- Pelvic only	3 (18.8%)	1 (12.5%)	
- PPaLNs	10 (62.5%)	7 (87.5%)	
LN involvement			
- Pelvic LNs	8 (50.0%)	5 (62.5%)	0.444
- Paraaortic LNs	3 (18.8%)	3 (37.5%)	0.302
Stage			
- I–II	5 (31.3%)	2 (25.0%)	0.572
- III–IV	11 (68.8%)	6 (75.0%)	
Adjuvant therapy			
- Observation ± VBT	3 (18.8%)	2 (25.0%)	
- EBRT ± VBT	2 (12.5%)	1 (12.5%)	0.480
- Chemotherapy ± VBT	4 (25.0%)	-	
- Chemotherapy + EBRT	7 (43.8%)	5 (62.5%)	
Time to recurrence after initial diagnosis	16.7 ± 10.1	20.3 ± 5.0	0.356
ILNR treatment			
- CT only	6 (37.5%)	2 (25.0%)	
- RT only	4 (25.0%)	1 (12.5%)	0.098
- Resection + CT or RT	1 (6.3%)	4 (50.0%)	
- RT + CT	5 (31.3%)	1 (12.5%)	

PRS: post-recurrence survival; LN: lymph node; PPaLN: pelvic paraaortic lymph node; VBT: vaginal brachytherapy; EBRT: external beam radiotherapy; ILNR: isolated lymph node recurrence; RT: radiotherapy; CT: chemotherapy; CA125: Cancer Antigen 125.

had advanced disease ($p = 0.572$). The time to recurrence after the initial diagnosis was shorter in the short-term PRS group, although the difference was not statistically significant (16.7 ± 10.1 months *vs.* 20.3 ± 5.0 months; $p = 0.356$). There were no significant differences in treatment for ILNR between the short-term and long-term PRS groups ($p = 0.098$).

Cox regression analysis was conducted to identify significant prognostic factors for duration of PRS (Table 3). Receiver operating characteristic analysis was conducted to determine cut-off values for nominal variables to identify patients with long-term PRS. The cut-off age was set at 60 years (AUC = 0.500), tumor size at 4.0 cm (AUC = 0.313) and DFS at 18 months (AUC = 0.691). These cut-off values were applied in the regression analysis. Univariate regression analysis identified the presence of grade 3 tumors (OR = 1.9, 95% CI = 1.1–3.4) as worse prognostic factors. Prolonged DFS (≥18 months) (OR = 0.2, 95% CI = 0.1–0.7), and resection during recurrence treatment (OR = 0.2, 95% CI = 0.1–0.9) were found as protective factors. However, multivariate Cox regression analysis did not identify any independent prognostic factors.

Fig. 1 presents survival data based on significant prognostic factors identified in the univariate logistic regression analysis of PRS. The 2-year PRS rates were 60.0%, 66.7% and 23.5% in patients with grades 1–3, respectively ($p = 0.062$)

TABLE 3. Cox regression analysis of prognostic factors of post-recurrence survival.

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*	OR	95% CI	*p*
Advanced age (≥60 yr)	1.3	0.4–4.1	0.593			
Large tumor (≥4 cm)	2.6	0.7–9.3	0.129			
High CA125 (≥35 U/mL)	2.0	0.7–5.7	0.162			
Grade 3	1.9	1.1–3.4	0.033	1.6	0.9–3.1	0.091
Lymphovascular space invasion	2.5	0.7–9.0	0.145			
Deep myometrial invasion	1.7	0.6–4.7	0.252			
PPaLND at initial diagnosis	0.6	0.3–1.2	0.189			
PLN involvement at initial diagnosis	1.3	0.5–3.8	0.514			
PaLN involvement at initial diagnosis	0.9	0.3–2.7	0.927			
Early stage at initial diagnosis (I–II)	0.7	0.2–2.2	0.652			
Adjuvant EBRT at initial diagnosis	1.4	0.4–5.1	0.566			
Adjuvant CT at initial diagnosis	1.2	0.4–3.5	0.630			
Prolonged DFS (≥18 mon)	0.2	0.1–0.7	0.012	0.4	0.1–1.2	0.115
PPaLN recurrence	0.8	0.5–1.4	0.612			
PaLN recurrence	1.1	0.3–4.0	0.846			
Recurrence therapy (resection)	0.2	0.1–0.9	0.045	0.3	0.1–1.8	0.217

OR: odds ratio; CI: confidence interval; PPaLND: pelvic paraaortic lymph node dissection; EBRT: external beam radiotherapy; CT: chemotherapy; DFS: disease-free survival; CA125: Cancer Antigen 125; PLN: Pelvic Lymph Node; PaLN: Paraaortic Lymph Node; PPaLN: Pelvic Paraaortic Lymph Node.

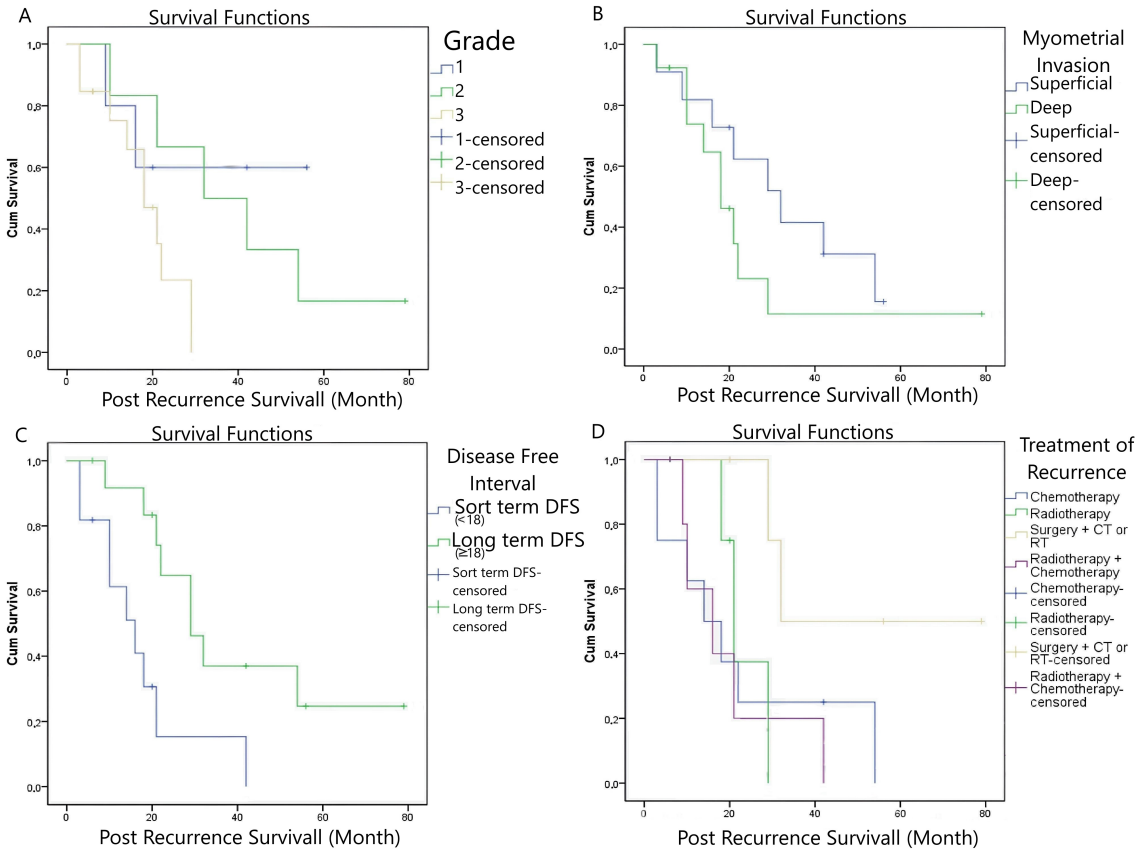

FIGURE 1. Kaplan-Meier analysis of post-recurrence survival according to (A) grade, (B) myometrial invasion, (C) DFS duration and (D) recurrence treatment. DFS: disease-free survival; RT: radiotherapy; CT: chemotherapy.

(Fig. 1A). Although patients with deep myometrial invasion had a lower 2-year PRS rate, the difference was not statistically significant (62.3% *vs.* 23.1%; $p = 0.235$) (Fig. 1B). The 2-year PRS rate was significantly lower in patients with shorter DFS (15.3%) than in those with longer DFS (64.8%) ($p = 0.007$) (Fig. 1C). Furthermore, the 2-year PRS rates were 25.0% for patients receiving only chemotherapy, 37.5% for those receiving only radiotherapy, 20.0% for those treated with a combination of chemotherapy and radiotherapy and 100% for those who underwent resection combined with chemotherapy or radiotherapy ($p = 0.129$) (Fig. 1D).

4. Discussion

Although lymphatic spread is common in EC, it typically occurs in conjunction with hematogenous metastasis, making isolated LN metastasis a rare occurrence. In our study of 24 patients with ILNR, 70.8% were initially diagnosed at an advanced stage (stage III–IV). As a result, approximately 80% of the patients received EBRT and/or chemotherapy. The mean time to recurrence was 17.9 ± 8.8 months. No significant independent prognostic factors were identified for long-term PRS.

Previous studies have demonstrated conflicting findings regarding the outcomes of patients with recurrent EC. Consensus treatment guidelines suggest that surgery and stereotactic radiotherapy can be considered for single or localized nodal recurrences if the recurrence is resectable. However, if the recurrence is considered unresectable, chemotherapy should be administered [7, 8]. Few studies have focused on ILNR and none have exclusively evaluated patients with endometrioid-type EC [9–11]. Therefore, a direct comparison between our findings and those of previous studies is not possible.

In a study by Ho *et al.* [9], which included 38 patients with ILNR due to EC, the most common histological types were endometrioid (42%) and serous (26%) tumors. At diagnosis, 55% of patients were in stages I–II. LN dissection was not performed in 34% of the patients, whereas pelvic lymphadenectomy and para-aortic lymphadenectomy were performed in 21% and 45% of cases, respectively. Among initial adjuvant treatments, 11% received brachytherapy and 42% received chemotherapy. Recurrence sites included PLNs (34%), PaLNs (21%) and PPaLNs (45%). OS was significantly worse for patients diagnosed at advanced stages (III–IV) (OR = 2.5, $p = 0.024$) and for those who received adjuvant chemotherapy (OR = 4.4, $p = 0.002$). However, the effects of histological type, grade, recurrence site and time to recurrence on OS were not statistically significant [9]. In our study, which exclusively focused on patients with endometrioid-type EC who developed ILNR, we found a lower proportion of early-stage patients at initial diagnosis (29%) relative to previous studies. This may be attributable to the lower recurrence risk typically associated with early-stage endometrioid tumors. Correspondingly, our rate of PPaLN dissection (70%) was higher, reflecting the advanced stage of most tumors in our cohort. The rates of LN metastasis were similar to those reported by Ho *et al.* [9]. When evaluating prognostic factors for long-term PRS, our univariate Cox regression analysis identified grade 3 tumors, prolonged DFS and resection as significant factors in recurrence treatment. This information was found to be consistent with the literature. In the literature, high grade, short DFS time, isolation of the recurrence and resectability are important points in the treatment of recurrence [4]. However, none of these variables were independent risk factors. It is possible that the small sample size limited the ability to detect independent prognostic factors. Nevertheless, based on studies of other recurrence types, prolonged DFS and resection, which are generally accepted as independent prognostic factors for long-term PRS, could also apply to patients with ILNR. Further prospective studies with larger patient cohorts are needed to confirm this hypothesis.

In the review by Kılıç *et al.* [10], which included data from 42 EC patients with peripheral LN metastasis, endometrioid cancer was the most common tumor type (31%). According to the 2009 International Federation of Gynecology and Obstetrics staging, 40% were stage I, 35% stage III and 11% stage IV. The first recurrence was detected as nodal metastasis in 95% of the patients; peripheral LN metastasis constituted 4.9% of all metastases. The most common recurrence sites were peripheral LNs (42%), inguinal nodes (26%) and supraclavicular nodes. PRS was 80% for patients who underwent surgical treatment, compared with 67% for those who did not ($p = 0.299$) [10]. No significant differences in PRS were found between patients who received chemotherapy and those who did not. Additionally, the 5-year PRS did not significantly differ based on initial stage ($p = 0.890$), histological type ($p = 0.577$) or DFS interval ($p = 0.339$). A significant limitation of this review was the use of diverse treatment algorithms across different centers. Furthermore, 17% of the patients did not have ILNR [10]. Therefore, our study, which focused on ILNR in patients with endometrioid-type EC, offers valuable insights.

In a study by Capasso *et al.* [11], the ILNR rate was 1.6%. The recurrence rates for isolated PLNs, isolated PaLNs, distant ILNR and multiple LN recurrences were 13.6%, 22.7%, 24.2% and 39.4%, respectively. Notably, 62.1% of the recurrences were endometrioid tumors, whereas 37.9% were non-endometrioid. At the time of diagnosis, 22.7% of the patients were in early stages (I–II), and 77.3% were in advanced stages (III–IV). The median time to recurrence was 1.0 year (range: 0.6–2.4 years). The median cause-specific survival after the diagnosis of ILNR was 2 years; there were no significant differences in survival rates among the four recurrence groups. Among the 15 patients with long-term PRS >5 years, seven had para-aortic recurrence, four had multiple recurrences (26.7%), three had distant LN recurrences and one had pelvic recurrence. Surgical resection was performed in 53.3% of these patients. The study concluded that surgical resection was independently associated with improved survival in cases of ILNR [11]. Cure was achieved after curative radiotherapy with volume modulated arc therapy in a patient with isolated mediastinal lymph node recurrence that developed 5 years after initial surgery and adjuvant chemotherapy. Cure can be seen even in distant lymph node metastases [12]. In particular, if recurrence occurs in a previously irradiated area, surgical resection alone may be appropriate; alternatively, radical resection combined with intraoperative radiotherapy or radiofrequency ablation could be considered viable options.

Surgical resection provides increased survival and cure in patients, as supported by our study and many recurrence studies. However, it should be noted that surgical applicability is not possible in every patient. Treatment decisions should be made by evaluating parameters such as tumor number, size and location of tumors, patient's age, performance status, body mass index (BMI), co-morbid conditions, surgeon availability and expertise.

The main limitation of this study was its retrospective design. The most important points in the retrospective study are the difficulty of patients to remember or to remember incorrectly and the difficulty of accessing the results. However, in our study, all the information is on the computer and our filing system is almost flawless. Therefore, despite this limitation, we can access all the information correctly. Although the small sample size presents a challenge, it reflects a relatively homogeneous population, particularly considering the focus on a specific patient group characterized by tumor type and isolated metastasis site. One of the weaknesses of the study is the lack of statistical power to draw definitive conclusions due to the small number of patients. The third important limitation is that the patients were spread over many years, which resulted in changes in the operating surgical team and updates in adjuvant treatment decisions.

5. Conclusions

In conclusion, although no independent prognostic factors for long-term PRS were identified in patients with ILNR after surgery for endometrioid-type EC, grade 3 tumors at initial surgery are possibly associated with worse outcomes. Prolonged DFS (>18 months) and surgical resection are possible predictors of better outcomes. Prospective studies are needed to better define prognostic factors. In particular, the effect of molecular patterns should be examined.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

KG and VG—designed the research study. İÇ and İAÖ—performed the research. VG and İÇ—analyzed the data. VG—wrote the manuscript. KG and İAÖ—edited. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics committee approval was received from Tepecik Research and Treatment Hospital for the study (Decision no: 2021/01-30), and all procedures adhered to the ethical standards outlined in the 1964 Helsinki declaration and its subsequent amendments or equivalent ethical standards. Informed consent was obtained from all subjects we could reach (retrospective study and due to the presence of deceased patients) who participated in the study.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA: A Cancer Journal for Clinicians. 2022; 72: 7–33.

[2] Perrone E, Capasso I, Pasciuto T, Gioè A, Gueli Alletti S, Restaino S, *et al*. Laparoscopic *vs.* robotic-assisted laparoscopy in endometrial cancer staging: large retrospective single-institution study. Journal of Gynecologic Oncology. 2021; 32: e45.

[3] Abu-Rustum NR, Chi DS, Leitao M, Oke EA, Hensley ML, Alektiar KM, *et al*. What is the incidence of isolated paraaortic nodal recurrence in grade 1 endometrial carcinoma? Gynecologic Oncology. 2008; 111: 46–48.

[4] Bradford LS, Rauh-Hain JA, Schorge J, Birrer MJ, Dizon DS. Advances in the management of recurrent endometrial cancer. American Journal of Clinical Oncology. 2015; 38: 206–212.

[5] Aloisi A, Casanova JM, Tseng JH, Seader KA, Nguyen NT, Alektiar KM, *et al*. Patterns of FIRST recurrence of stage IIIC1 endometrial cancer with no PARAAORTIC nodal assessment. Gynecologic Oncology. 2018; 151: 395–400.

[6] Tubridy EA, Taunk NK, Ko EM. Treatment of node-positive endometrial cancer: chemotherapy, radiation, immunotherapy, and targeted therapy. Current Treatment Options in Oncology. 2024; 25: 330–345.

[7] Restaino S, Dinoi G, La Fera E, Gui B, Cappuccio S, Campitelli M, *et al*. Recurrent endometrial cancer: which is the best treatment? Systematic review of the literature. Cancers. 2022; 14: 4176.

[8] Nakamura H, Takehara K, Samura O, Mizunoe T. Cytoreductive surgery for isolated para-aortic lymph node recurrence of endometrial cancer: report of four cases and a review of the literature. European Journal of Gynaecological Oncology. 2014; 35: 535–538.

[9] Ho JC, Allen PK, Jhingran A, Westin SN, Lu KH, Eifel PJ, *et al*. Management of nodal recurrences of endometrial cancer with IMRT. Gynecologic Oncology. 2015; 139: 40–46.

[10] Kılıç F, Kimyon Cömert G, Akar S, Kılıç C, Çakır C, Yüksel D, *et al*. Evaluation of peripheral nodal recurrence in patients with endometrial cancer. Journal of the Turkish-German Gynecological Association. 2022; 23: 38–50.

[11] Capasso I, Garzon S, Kumar S, Weaver AL, Mc Gree M, De Vitis LA, *et al*. Prognostic factors in patients with endometrial cancer with isolated lymphatic recurrence. International Journal of Gynecological Cancer. 2023; 33: 1169–1178.

[12] Montanelli L, Reato C, Mauro S, Meregalli S, Spallino M, Buda A. A rare case report: isolated mediastinal lymph node recurrence in high-risk endometrial cancer at 5 years after primary laparoscopic surgery. Journal of Minimally Invasive Gynecology. 2018; 25: 537–540.

How to cite this article: Varol Gülseren, İlker Çakır, İsa Aykut Özdemir, Kemal Güngördük. Isolated lymph node recurrence and prognosis in endometrioid type endometrial cancer. European Journal of Gynaecological Oncology. 2025; 46(2): 85-91. doi: 10.22514/ejgo.2025.024.