



# Impact of lymph node staging techniques on lymphedema and quality of life in early-stage endometrial cancer: A prospective cohort study

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## ABSTRACT

**Background:** Sentinel lymph node (SLN) biopsy is increasingly replacing complete pelvic lymphadenectomy (CL) for staging early-stage endometrial cancer (EC), but its long-term impact on patients' quality of life (QoL) and lymphedema remains underexplored.

**Objective:** To compare overall health perception (oHP), health-related QoL (HRQoL), and symptomatic lymphedema in patients staged with SLN versus CL. Secondary objectives included the assessment of symptomatic lymphedema and surgical complications.

**Methods:** We conducted a prospective single-center observational study including 97 patients treated early-stage EC, with 50 undergoing SLN plus CL and 47 undergoing SLN only. Patients completed EQ-5D-3L, oHP scale (0–100), and the self-reported lower-extremity lymphedema questionnaire (LELQ) at baseline and 6-month follow-up. Multivariate analysis adjusted for confounders including surgical approach and adjuvant therapy.

**Results:** At 6 months, the SLN group reported significantly better oHP (median 85 vs. 70;  $p = 0.001$ ) and HRQoL impairment (median score 5 vs. 7;  $p = 0.001$ ) than the CL group. Symptomatic lymphedema (LELQ > 5) was significantly lower in the SLN group (7.0 %) than in the CL group (34.4 %,  $p = 0.002$ ). No significant differences in intra- or postoperative complications were observed.

**Conclusion:** SLN biopsy was associated with improved QoL and lower incidence of lymphedema compared to complete lymphadenectomy. These findings support the use of SLN mapping as the preferred nodal staging technique to minimize morbidity and enhance survivorship outcomes in early-stage EC patients.

## 1. Introduction

The World Health Organization (WHO) defines health as a state of complete physical, mental, and social well-being. Based on this definition, quality of life (QoL) is considered an integral component of health status among cancer survivors. Endometrial cancer (EC) is the most common malignancy of the female genital tract in high-income countries, with a 132 % increase in incidence over the past 30 years (Crosbie et al., 2022). Fortunately, patients diagnosed at stage I have an overall survival rate greater than 90 %, making EC one of the cancers with the highest number of long-term survivors, following breast cancer (Miller et al., 2022). Although most cases are diagnosed in women over 55 years old, it is important to note that approximately 14 % of cases occur in younger women, under the age of 40, at the time of diagnosis ("The

Statistical Office of the European Union.", 2017). Cancer survivors often experience lasting side effects from treatment, which may significantly impact their psychological well-being by constantly reminding them of their cancer history (Sanjida et al., 2021; Neron et al., 2019). Given that life expectancy for women in Europe ranges from 81 to 85 years the impact of treatment on their QoL may persist for decades ("The Statistical Office of the European Union.", 2017). This, in turn, may influence their psychological well-being and, as a result, impact their overall health status as defined by the WHO.

It is important to emphasize that QoL is a critical concern for all patients, regardless of age or expected survival time. Therefore, preserving QoL should be a priority for all individuals diagnosed with EC.

Performing a lymphadenectomy in EC patients primarily aims to stage the disease (Concin et al., 2021), with no demonstrated impact on

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<https://doi.org/10.1016/j.gore.2025.101919>

Received 24 June 2025; Received in revised form 28 July 2025; Accepted 31 July 2025

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survival (ASTEC study group, 2009, Panici et al., 2008). For this reason, sentinel lymph node (SLN) biopsy has been introduced in leading clinical guidelines over the past decade as a staging technique for early-stage EC (Concin et al., 2021; Holloway et al., 2017; Koh et al., 2018). Several studies have demonstrated that SLN biopsy is associated with lower morbidity and reduced rates of lymphedema (Accorsi et al., 2020). There is currently no evidence to suggest that SLN biopsy has better outcomes in terms of impact on QoL than complete pelvic lymphadenectomy (CL). The hypothesis is that SLN biopsy has a less pronounced negative impact on the postoperative QoL for women with an early-stage EC, compared to CL.

Therefore, the main objective of this prospective study is to assess the QoL of patients with early-stage EC based on the lymph node staging technique (SLN vs. SLN plus CL).

## 2. Objectives

**Primary Objective:** To assess the impact on overall health perception (oHP) and health-related quality of life (HRQoL) in patients surgically treated for early-stage EC, based on the lymph node staging technique used: pelvic SLN biopsy versus SLN with complete pelvic lymphadenectomy (CL).

**Secondary Objectives:** To evaluate the incidence of symptomatic lymphedema and assess intraoperative and postoperative complications between both groups.

## 3. Materials and methods

### 3.1. Study design

This was a prospective, longitudinal, single-center study involving two cohorts of patients with early-stage endometrial cancer (EC), treated surgically at a tertiary-level hospital using a minimally invasive approach (laparoscopy/robot-assisted surgery). The initial cohort of patients (January 2019 to March 2020) was included during the institutional validation phase of the sentinel lymph node (SLN) technique. During this phase, SLN biopsy was systematically followed by complete pelvic lymphadenectomy (CL) to confirm the accuracy of SLN mapping. After validation, SLN biopsy became the standard of care for nodal staging in early-stage EC at our center. From March 2020 onward, robotic surgery replaced laparoscopy as the standard minimally invasive approach. Our group's findings are detailed in an article published in Cancers in 2022 (Torrent et al., 2022).

### 3.2. Participants

A total of 97 patients diagnosed preoperative with early-stage EC, who underwent primary surgical treatment between January 2019 and November 2022, were included and divided into two groups based on the type of nodal assessment performed during the primary surgical treatment: **CL Group** (SLN plus CL): 50 patients included during the validation period of the SLN technique in our center (SLN biopsy was first performed, followed by CL) and those at high histological risk in which clinical guidelines recommend performing CL after SLN (de Ginecológia et al., 2023); **SLN Group** (SLN only): 47 patients, including those with preoperative diagnoses of endometrial intraepithelial neoplasia (EIN), later confirmed as EC postoperatively, and those included after validation of the SLN technique (Flow chart in Fig. 1).

In cases where intraoperative SLN analysis indicated nodal involvement, pelvic and para-aortic lymphadenectomy (from the aortic bifurcation to the left renal vein) was performed. Clinical and demographic characteristics of the study population are presented in Table 2.

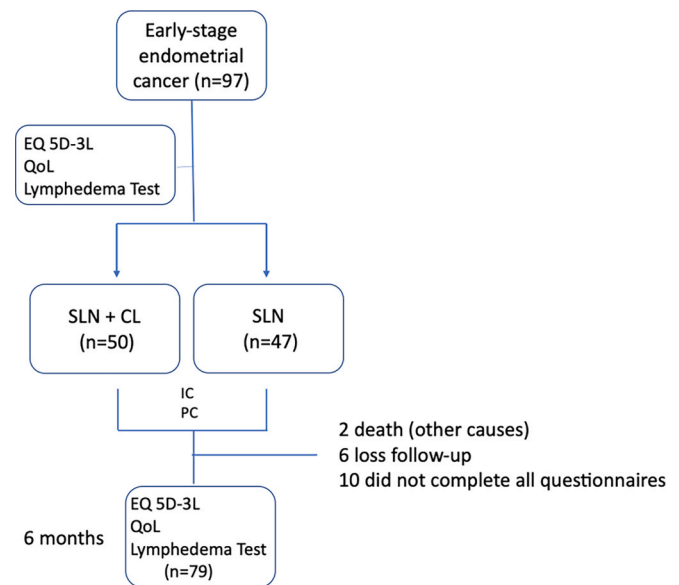


Fig. 1. Flowchart of participants. QoL: Quality of Life; SLN: Sentinel Lymph Node; CL: Complete Lymphadenectomy; IC: Intraoperative Complications; PC: Postoperative Complications.

### 3.3. Surgical approach

All women underwent minimally invasive surgery (MIS). Laparoscopic approach (KarlStorz Endoscope, Tuttlingen, Germany) was performed from January 2019 to March 2020. From March 2020 robotic surgery was introduced in our center (da Vinci® Surgical System Version Xi, Intuitive Surgical Inc., Sunnyvale, CA, USA). Therefore, from early 2020 onwards, all patients underwent robotic surgery.

### 3.4. Patient-report outcome

Two surveys were administered before surgery and at the 6-month follow-up. Patients completed the following questionnaires: a) HRQoL: Assessed using the EQ-5D-3L questionnaire (scores range from 5 to 15, with higher scores indicating worse QoL (Law et al., 2018); b) oHP: evaluated on a scale from 0 to 100, with higher scores indicating better health perception. At the 6-month follow-up, patients also completed the Self-Report Lower-Extremity Lymphedema Questionnaire (LELQ), developed by Yost et al., which measures lymphedema-related symptoms (Yost et al., 2013). Scores range from 0 to 52, with a score of  $\geq 5$  indicating positive lymphedema.

The EQ-5D-3L questionnaire covers five health dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (Law et al., 2018). Each dimension is scored on three levels: no problems, some problems, and extreme problems. In this study, we analysed the distribution of responses across these dimensions to better understand the specific areas of QoL affected by the surgical approach. To compare the impact on QoL and oHP between groups, the scores from both questionnaires reported by each patient were analyzed.

Lymphedema cases and intra- and postoperative complications were recorded for each group. Intra- and post-operative complications collected included bladder injury, intestinal injury, anesthetic complications, surgical wound infection, over-infected lymphocele, obturator nerve neuropathy, fever, and others. These were classified using the ClassIntra and Clavien-Dindo classification systems. For lymphocele diagnosis, a thoracoabdominal CT scan was performed at six months. Inclusion and exclusion criteria are described in Table 1.

Patients who died during the study were excluded because they did not complete the 6-month follow-up questionnaires, which were essential for evaluating our primary outcomes.

**Table 1**

Inclusion and exclusion criteria. ICG: Indocyanine Green; TC99m: Technetium-99 m.

Inclusion Criteria:	
<ul style="list-style-type: none"> <li>• Histological diagnosis of endometrial adenocarcinoma.</li> <li>• Endometrial intraepithelial neoplasia (EIN), later confirmed as EC postoperatively</li> <li>• Diagnosis of early-stage disease (FIGO stage I-II) confirmed by imaging studies.</li> <li>• Absence of extrauterine disease.</li> </ul>	
Exclusion Criteria:	
<ul style="list-style-type: none"> <li>• Contraindication for surgical treatment.</li> <li>• Contraindication for ICG and/or Tc99m injection.</li> <li>• Patients with a history of pelvic or abdominal radiotherapy.</li> <li>• Patients who die during the study, either due to the disease or other medical conditions</li> <li>• EIN not confirmed as EC postoperatively</li> </ul>	

**Table 2**

Clinical and Demographic Characteristics of the Study Population (n = 97).

		Total n = 97(%)	CL + SLN (%) (n = 50)	SLN (n = 47)	P
Age		62.0 (56.0–71.0)	64.5 (56.0–74.0)	61.0 (56.0 – 70.0)	0.392
BMI		30.0 (25.0–37.0)	30.0 (25.0–36.0)	30.0 (25.0–37.0)	0.54
	BMI < 30	44 (45.4 %)	24 (48 %)	20 (42.6 %)	0.590
	BMI ≥/ > 30	53 (54.6 %)	26 (52 %)	27 (57.4 %)	
Surgical approach	Laparoscopic	32 (33 %)	26 (52 %)	6 (12.8 %)	<0.001
	Robotics	65 (67.0 %)	24 (48.0 %)	41 (87.2 %)	
Histological type	Endometrioid	71 (73.2 %)	35 (70 %)	36 (76.6 %)	NA
	Serous	13 (13.4 %)	10 (20 %)	3 (6.4 %)	
	Clear cell	2 (2.1 %)	1 (2 %)	1 (2.1 %)	
	Carcinosarcoma	6 (6.2 %)	4 (8.0 %)	2 (4.3 %)	
	Others	5 (5.2 %)	0 (0.0 %)	5 (10.6 %)	
ESGO/ESTRO/ESP Risk group	Low	37 (38.1 %)	16 (32.0 %)	21 (44.7 %)	NA
	Intermediate	29 (29.9 %)	10 (20 %)	19 (40.4 %)	
	High-intermediate	31 (31.3 %)	24 (48 %)	7 (14.9 %)	
Adjuvant Therapy	No	37 (38.9 %)	14 (28 %)	24 (51.1 %)	0.018
	Yes	60 (61.8 %)	36 (72 %)	23 (48.9 %)	
Para-aortic lymphadenectomy	No	57 (58.8 %)	19 (38 %)	38 (80.9 %)	<0.001
	Yes	40 (41.2 %)	31 (62 %)	9 (19.1 %)	

NA: p-value not calculated due to small sample size and low frequency in some subcategories, which may limit the reliability of a global Chi-square test.

BMI: Body Mass Index; ESGO/ESTRO/ESP: European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology; European Society of Pathology; CL: Complete Lymphadenectomy; SLN: Sentinel Lymph Node biopsy.

Preoperative assessment included transvaginal ultrasound and magnetic resonance imaging (MRI) to assess myometrial invasion. In high-risk patients, a thoracoabdominal CT was performed.

All patients signed a specific consent form. The present study was approved by the local Ethics Committee of Balearic Islands, Spain (CEI-IB. Ref. IB 4103/20 PI). Patients' data were collected prospectively during the study by the investigation team (A.T., A.S., A.R. and L.F.).

### 3.5. Data analysis

A descriptive analysis of all variables was performed to define the characteristics of the study group, using frequencies and percentages for qualitative variables and median and interquartile range for numerical variables. Comparisons between the two groups were made using the Mann-Whitney *U* test for quantitative variables and the Chi-square test or Fisher's exact test for categorical variables. To analyze the possible association of complications with other variables, multivariate regression methods were applied to eliminate potential confounding factors. A p-value of < 0.05 was considered statistically significant.

A complete case analysis was performed for patient-reported outcomes, including only those who completed both baseline and 6-month follow-up questionnaires. To assess potential attrition bias, a comparative analysis of baseline demographic and clinical characteristics was

conducted between patients who completed follow-up and those who lost follow-up.

Data analysis was conducted by the Methodological and Statistical Support Platform of the Health Research Institute of the Balearic Islands. The statistical software used for data analysis was IBM-SPSS v.26 (SPSS Inc., Chicago, IL, USA).

## 4. Results

A total of 97 patients were included, with 50 (51.5 %) undergoing CL and 47 (48.5 %) undergoing pelvic SLN biopsy (Flowchart, Fig. 1). Both groups were similar in terms of age, BMI, histological type, and ESGO/ESTRO/ESP risk group, with no statistically significant differences observed. Clinical and demographic features are presented in Table 2.

At six months, 79 out of 97 patients (81.4 %) completed all three questionnaires (43 (54.4 %) in the SLN group and 36 (45.6 %) in the CL group). The patient's loss rate was 18.5 % and were excluded from the final analysis due to death or incomplete data.

No statistically significant differences were found between patients lost to follow-up (n = 18) and those included in the final analysis (n = 79) in terms of age, BMI, histological type, or ESGO/ESTRO/ESP risk group. These findings suggest that losses occurred at random and are unlikely to have introduced significant bias (Table 3).

**Table 3**  
Baseline Characteristics of Patients Lost to Follow-Up vs. Final Cohort (n = 79).

		N = 18	N = 79	P
Age		66.5 (56.0–77.0)	62.0 (56.0–71.0)	<b>0.414</b>
BMI		27.0 (25.0–36.0)	30.0 (26.0–37.0)	<b>0.198</b>
	BMI < 30	10 (55.0 %)	34 (43.0 %)	<b>0.336</b>
	BMI ≥ 30	8 (44.4 %)	45 (57.0 %)	
Surgical approach	Laparoscopic	9 (50.0 %)	23 (29.1 %)	<b>0.089</b>
	Robotic	9 (50.0 %)	56 (70.9 %)	
Histological type	Endometrioid	12 (66.7 %)	59 (74.7 %)	<b>0.488</b>
	Non-Endometrioid	6 (33.3 %)	20 (25.3 %)	
ESGO/ESTRO/ESP	Low	5 (27.8 %)	32 (40.5 %)	<b>0.316</b>
Risk group	Intermediate-High	13 (72.2 %)	47 (59.5 %)	
	Low-Intermediate	10 (55.6 %)	56 (70.9 %)	<b>0.208</b>
	High-intermediate and High	8 (44.4 %)	23 (29.1 %)	
Adjuvant Therapy	No	11/17 (64.7 %)	48/78 (61.5 %)	<b>0.807</b>
	Yes	6/17 (35.3 %)	30/78 (38.5 %)	
Para-aortic lymphadenectomy	No	8 (44.4 %)	49 (62.0 %)	<b>0.171</b>
	Yes	10 (55.6 %)	30 (38.0 %)	

BMI: Body Mass Index; ESGO/ESTRO/ESP: European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology; European Society of Pathology.

A post-hoc power analysis was conducted based on the observed effect sizes. The statistical power to detect differences at a 0.05 significance level was 98 % for the HR-QoL score, 50 % for oHP, and 100 % for lymphedema screening (LELQ).

#### 4.1. Intra-operative and post-operative complications (Table 4)

All intraoperative complications (3.1 %) were recorded in the CL group (three complications). However, there were no statistically significant differences between the two groups regarding intraoperative ( $p = 0.243$ ) or postoperative complications ( $p = 0.833$ ). Among the post-operative complications (eleven patients; 11.3 %), six (12 %) were in the CL group and five (10.6 %) in the SLN group. Notably, there were four cases (two in each group) of decreased sensitivity in the inner thigh area and reduced adduction, indicative of obturator nerve neuropathy. All obturator nerve injuries were thermal; none were due to partial or total nerve section. Three cases resolved with rehabilitation, with patients asymptomatic at six months, while one case (in the SLN group) had mild

**Table 4**

Intra and post-operative complications. ClassIntra: intraoperative complications classifications (Dell-Kuster et al., 2020). Clavien-Dindo: Post-Operative complications classification (Dindo et al., 2004).

Complications	Total	CL + SLN, n (%)	SLN, n (%)	P
Intraop. Complications (ClassIntra)	3 (3.1 %)	3 (6.0 %)	0 (0 %)	<b>0.243</b>
Bladder injury (II)	1	1	0	
Intestinal injury (II)	1	1	0	
Anaesthetic complication (I)	1	1	0	
Post-op. Complications (Clavien-Dindo)	11 (11.3 %)	6 (12.0 %)	5 (10.6 %)	<b>0.833</b>
Surgical wound infection (I)	4	2	2	
Over-infected lymphocele (III)	2	2	0	
Obturator nerve neuropathy (I-II)	4	2	2	
Fever (I)	1	0	1	

Intraop: Intraoperative; Post-op: Postoperative; CL: Complete Pelvic Lymphadenectomy; SLN Sentinel Lymph Node Biopsy.

symptoms persisting at six months post-surgery.

#### 4.2. Results of the HR-QoL questionnaire and oHP (Fig. 2)

According to HR-QoL assessment (Questionnaire EQ-5D-3L), the SNL group had significantly better results, which included less impact on morbidity, self-care, daily activities and pain (HR-QoL 5 vs 7,  $p = 0.001$ ), Table 5. A total of 61.1 % of patients in the CL group reported a deterioration in their perception of HR-QoL at six months post-surgery, compared to 37.2 % in the SLN group (Fig. 2) Regarding the oHP, the CL group had significantly worse oHP at six months post-surgery compared to the SLN group (85 vs 70,  $p = 0.001$ ), Table 5. Additionally, when comparing oHP between 0–6 months in both groups, the differences were also statistically significant (median of  $-7.5$  in the CL group vs median of 0 in the SLN group,  $p = 0.011$ ). A multiple regression analysis, considering potential confounding factors such as the addition of para-aortic lymphadenectomy, robotic surgery, and adjuvant treatment, showed that the SLN group had a lower risk of worsening oHP at six months post-surgery (OR 0.208, 95 % CI 0.063–0.688,  $p = 0.010$ ).

#### 4.3. Results of self-report lower-extremity lymphedema questionnaire (LELQ) (Fig. 3)

A positive LELQ score (greater than five) was observed in 34.4 % of patients in the CL group and 7.0 % of patients in the SLN group ( $p = 0.002$ ). In the multiple regression analysis, considering the same confounding factors as those used for HR-QoL and oHP, the SLN group showed a lower risk of lymphedema compared to the CL group (OR 0.096 [0.020–0.459],  $p = 0.003$ ).

During the first six months post-surgery, five patients (5.2 %) developed lymphedema, and three patients (3.1 %) developed lymphocele, all of whom were in the CL group.

#### 4.4. Impact of body mass index (BMI)

Most lymphedemas (80 %) and lymphoceles (66.7 %) were diagnosed in patients with a BMI < 30, with no differences in lymphedema screening (symptoms). In our series, obesity (BMI > 30) was associated with a worsening of HRQoL (62.9 % vs 37.1 %) and oHP (57.9 % vs 42.1 %), although these differences did not reach statistical significance ( $p > 0.05$ ).

#### 4.5. Impact of para-aortic lymphadenectomy

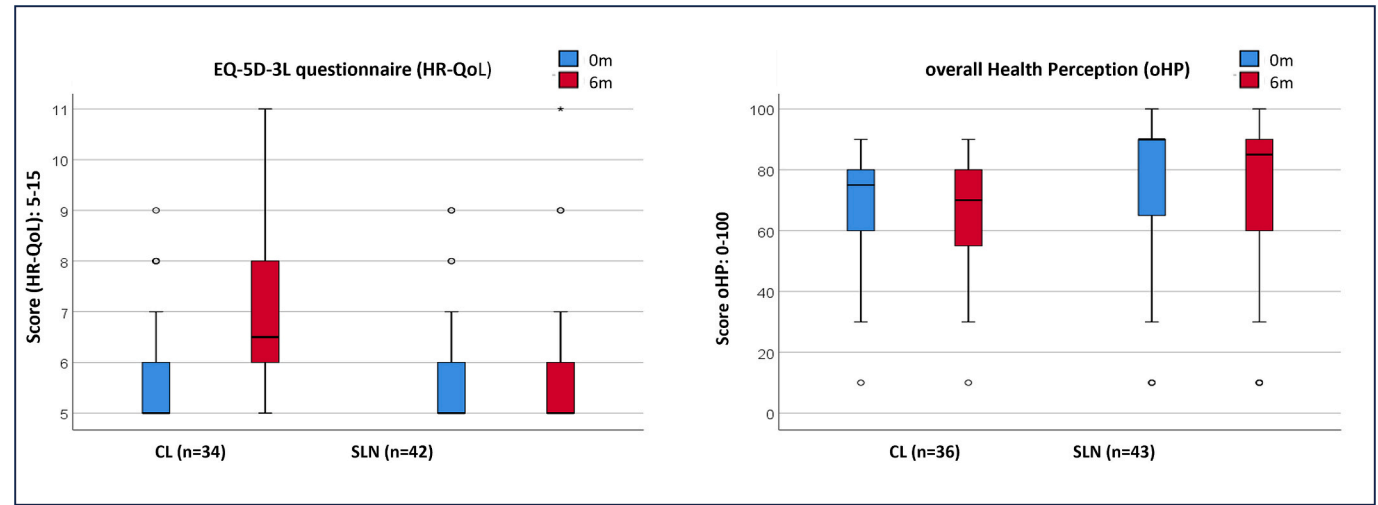
In the CL group, more para-aortic lymphadenectomies were performed (62 %) compared to the SLN group (19.1 %) ( $p = 0.000$ ). However, in the multiple regression analysis, the addition of a para-aortic lymphadenectomy to any staging technique was not associated with a greater risk of lymphedema (OR 1.750 [0.559–5.481],  $p = 0.337$ ) or a worsening of either HRQoL (OR 1.024 [0.402–2.609],  $p = 0.960$ ) or oHP (OR 1.744 [0.697–4.364],  $p = 0.235$ ).

#### 4.6. Impact of adjuvant treatment

In the CL group, 73.5 % received adjuvant treatment after surgery (brachytherapy and/or external radiotherapy with or without chemotherapy). In the SLN group, 50.0 % received complementary treatment ( $p = 0.018$ ). Among the patients who scored positively (>5) on the LELQ, 80 % (12/15) had received adjuvant treatment, compared to only 20 % (3/15) of patients who did not receive complementary treatment. However, the differences were not significant ( $p = 0.093$ ), likely due to the small sample size.

## 5. Discussion

Despite the growing evidence of SLN mapping in endometrial cancer



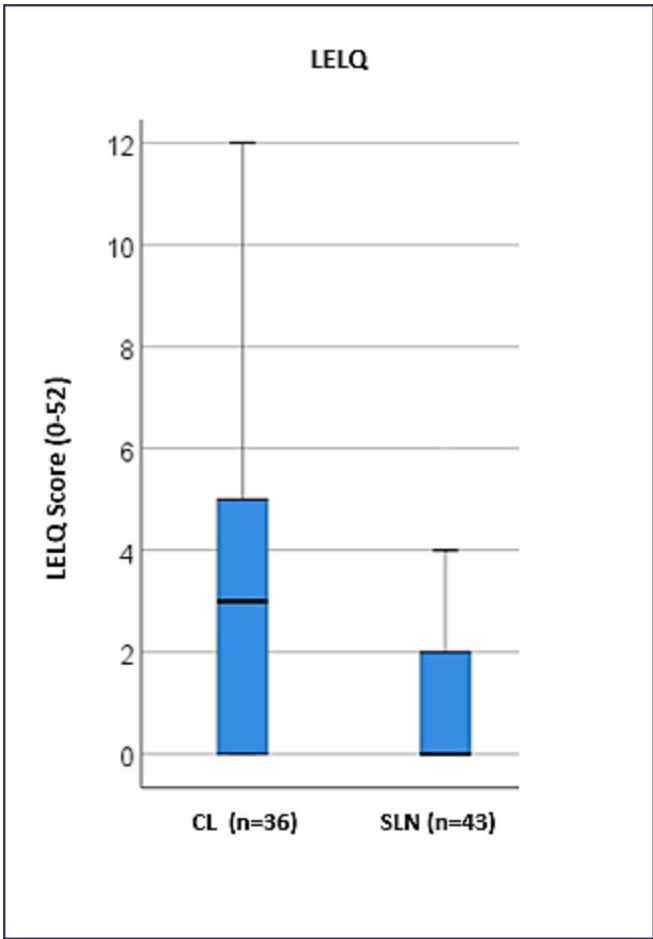
**Fig. 2.** Box Plot Health Related Quality of life (HR-QoL) and Overall Health Perception (oHP). Blue: 0 months; Red: 6 months. Note: The Y-axis represents the score ranges of the questionnaires. HR-QoL (EQ-5D-3L) ranges from 5 to 15 (higher scores = worse quality of life). oHP ranges from 0 to 100 (higher scores = better health perception).

**Table 5**  
EQ-5D-3L-Health-Related Quality of Life Questionnaire, oHP and LELQ scores according to nodal staging. Diff: Difference between 0 and 6 months; oHP: overall Health Perception; LLELQ: Self-report lower Extremity Lymphedema Questionnaire.

EQ-5D-3L	Total	CL + SLN, n (%)	SLN,n(%)	p
N	79	36 (45.6 %)	43 (51.4 %)	
Median at 6 months	6.0 (5.0–7.0)	7.0 (6.0–8.0)	5.0 (5.0–6.0)	<b>0.001</b>
Diff (0–6 months)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	0.0 (0.0–1.0)	<b>0.012</b>
EQ-5D-3L worsening	38/79 (48.1 %)	22/36 (61.1 %)	16/43 (37.2 %)	<b>0.044</b>
<b>oHP</b>				
Median at 6 months	80 (60–85)	70 (60–80)	85 (60–90)	<b>0.001</b>
Diff (0–6 months)	0 (–10–0)	–7.5 (–10–0)	0.0 (–10–0)	<b>0.011</b>
oHP worsening	38/79 (48.1 %)	25/36 (69.4 %)	13/43 (30.2 %)	<b>0.001</b>
<b>LELQ median</b>				
Median 6 months	1 (0–4)	3 (0–5)	0 (0–2)	<b>0.006</b>
Score > 5	16/79 (20.2 %)	13/36 (36.1 %)	3/43 (7.0 %)	<b>0.002</b>

(EC)(Rossi et al., 2017), many studies have shown a lower incidence of lymphedema (Cucinella et al., 2024; Moffatt et al., 2025 Jun 10), but few prospective studies analyze the impact on quality of life (QoL) (Sanjida et al., 2021; Lee et al., 2021). One of the main prospective studies comparing the incidence of lymphedema in women with EC undergoing SLN biopsy versus CL was published in 2018 by Geppert et al. (Geppert et al., 2018). SLN alone resulted in a lower incidence of leg lymphedema than CL (1.3 % vs 18.1 %,  $p = 0.0003$ ). This study did not assess the impact on QoL of having lymphedema, and all patients in the CL group also underwent *para*-aortic lymphadenectomy in addition to CL. In our series, patients who underwent *para*-aortic lymphadenectomy did not show statistically significant differences in LELQ, HR-QoL, or oHP.

The LELQ was administered at the 6-month follow-up visit because our primary objective was to evaluate the early postoperative impact of LN staging techniques. This time point was selected based on prior studies indicating that symptomatic lymphedema typically emerges within the first few months after surgery. In our clinical setting, the first postoperative visit is usually scheduled one month after surgery, and the 6-month follow-up is the standard recommended time for assessing early



**Fig. 3.** Box Plot Self-Report Lower- Extremity Lymphedema Questionnaire (LELQ).

postoperative outcomes, including lymphedema. We acknowledge that longer-term follow-up may provide additional insights.

The results obtained in the QoL assessment were calculated considering the patient loss rate (18.5 %) were unable to complete all the



questionnaires (death or incomplete data). At 6 months, 79 patients completed all questionnaires. Although patients with incomplete data (18.5 %) were excluded from the final analysis, we acknowledge that this may introduce potential bias, as these patients could differ in relevant clinical or psychosocial characteristics.

Concerning the histological type, CL group showed a significantly higher proportion of serous carcinoma than SLN group (20 % vs. 6.4 %). CL group is composed of patients included during the SLN validation technique at our center (SLN followed by CL), and those at high histological risk in which clinical guidelines recommend performing lymphadenectomy after SLN (de Ginecología et al., 2023). Finally, the two groups were well-balanced, ensuring that the results were unaffected.

The hypothesis that CL negatively affects the overall perception of QoL in patients still lacks substantial evidence. In the prospective study by Wedin M et al. (Wedin et al., 2022) the HRQoL and lymphedema-specific QoL at twelve months were compared in patients treated for early-stage EC who underwent CL versus those who did not undergo any lymph node excision. Unlike our study, patients who underwent lymphadenectomy did not seem to experience an adverse effect on generic HRQoL. The presence of lower limb lymphedema negatively affected lymphedema-specific HRQoL, mainly in physical and functional domains, but had no impact on generic HRQoL.

In 2023, the first prospective study evaluating lymphedema and QoL comparing SLN mapping (74.3 % of patients) and SLN with the addition of lymphadenectomy (25.7 % of patients) in EC was published (Goncalves et al., 2023). They noted, similar to our study, a higher rate of lymphedema after lymphadenectomy but no difference was found in overall QoL between both groups based on objective measures (perimetry). However, they reported higher lymphedema symptom scores in the SLN + LND group using patient-reported outcomes, which aligns with our findings and reinforces the value of subjective assessment tool in evaluating survivorship impact. Our study is also prospective, and we found statistically significant differences favoring higher oHP and less impact on HRQoL in the SLN group compared to the CL group. Additionally, in our study, the sample sizes of both groups are more similar (48.5 % vs 51.5 % CL group) than in other studies.

To our knowledge, there is no universally established minimum clinically important difference (MCID) specifically defined for the oHP scale (0–100) or for the EQ-5D-3L index used to assess HRQoL in patients with endometrial cancer. However, previous studies using the EQ-5D-3L in oncology settings have suggested that a change of approximately 0.07–0.10 in the index score or a 1-point difference in the summary score may be considered clinically meaningful (Law et al., 2018).

We observed a median difference of 2 points in HRQoL scores (7 vs. 5;  $p = 0.001$ ) and a 15-point difference in oHP scores (70 vs. 85;  $p = 0.001$ ) between the CL and SLN groups at 6 months. These differences are not only statistically significant but also likely to be clinically relevant, especially considering the impact on patients' daily well-being.

The ongoing Chinese phase III multicenter randomized INSEC trial is currently recruiting patients and is expected to provide stronger evidence due to its robust design and large sample size. The study aims to enroll 722 patients randomized to either SLN biopsy alone or SLN biopsy plus complete lymphadenectomy (Deng et al., 2023).

In our series, the diagnosis of lymphedema (10 % in the CL group vs 0 % in the SLN group) is lower than reported in the literature. However, it is important to note that in our study, lymphedema was only explored if the lymphedema test scored more than five, as we aimed to assess the impact on the patient's QoL rather than visual lymphedema rates. These lymphedema rates are significantly lower in the SLN group (0 % compared to 10 % in the CL group, five patients;  $p = 0.057$ ) and remain much lower than in other studies (Law et al., 2018; Goncalves et al., 2023). The overall rate of lymphocele at six months was 3.1 % (three patients), all of whom were in the group that underwent systematic lymphadenectomy. Therefore, the lymphocele rate in the CL group is 6 % (three patients) compared to none (0 %) in the SLN group. Although the differences are not statistically significant ( $p = 0.243$ ), it is

noteworthy that two patients diagnosed with lymphocele required laparoscopic or radio-guided drainage (Clavien-Dindo grade III complication).

García-Pineda et al. ( $n = 90$ ) did not find statistically significant differences in overall QoL when comparing their CL group (67.8 %) with the SLN group (32.2 %). However, the SLN group had significantly less impact on patients' functional and symptom scores than the lymphadenectomy group (García-Pineda et al., 2023). In addition, their SLN group presented significantly less post-treatment pain.

Regarding surgical approach, the multiple regression analysis does not consider robotic surgery (RS) to be a confounding factor. Our hospital has a long-standing tradition of performing laparoscopic surgery (LS). RS was introduced at the beginning of 2020, and the advantages that offers in obese patients, such as EC patients (Asanoma et al., 2022), motivated us to perform RS on all patients.

Since we are an expert center in LS and RS, our goal was not to compare the two techniques, as they have already been published in different studies (Mäenpää et al., 2025; Madhuri and Butler-Manuel, 2017 Jun 1).

Other risk factors, such as obesity and age, can influence QoL scales. A study by Karatasli et al. investigated the impact of BMI on the QoL of patients with EC and concluded that the group with morbid obesity had poorer physical functioning than the group without morbid obesity ( $p < 0.011$ ) (Karatasli et al., 2021). In our series, patients with a BMI  $> 30$  showed a worsening of HR-QoL (62.9 % vs 37.1 %;  $p = 0.308$ ) and worse oHP (57.9 % vs 42.1 %;  $p = 0.872$ ). Most lymphedemas (80 %) and lymphoceles (66.7 %) were diagnosed in patients with a BMI  $< 30$ , but there were no differences in the LELQ, which reflects lymphedema symptoms.

Most patients in the SLN group are low and intermediate risk endometrial cancer than CL group (85.1 % vs. 52 %). Therefore, are expected that a lower rate of SLN group received adjuvant treatment than CL group (73.5 % vs 50 %). It should be noted that the majority of SLN group only received brachytherapy (70 %) and 20 % EBRT plus BT.

24 out of 31 patients with intermediate-high and high-risk endometrial cancer belong to the CL group, while only 22.6 % belong to the SLN group. This difference could explain why the CL group has a high percentage of patients receiving adjuvant treatment (73.5 %).

Our group has not investigated whether there is a correlation between lymphedema and the adjuvant treatment received due to our small sample. This topic has already been published by Lee in a large series (Lee et al., 2021). Lymphedema incidence was markedly higher in endometrial cancer according to the adjuvant treatment protocol, compared to the group that received surgery alone. The group that received radiotherapy alone or chemotherapy alone had a higher risk of lymphedema.

Pelvic radiation has been suggested as an important risk factor for lymphedema although other authors did not find post-operative radiation to be a predictive factor for lymphedema. In our series, after multivariate analysis, 80 % (12 patients) of those with an LELQ score  $> 5$  (symptomatic lymphedema) had received complementary treatment (brachytherapy/external radiotherapy with or without chemotherapy), whereas only 20 % of patients who had not received complementary treatment scored positively on the LELQ. These differences were not statistically significant ( $p = 0.093$ ), likely due to the small number of cases in both groups.

In the multiple regression analysis, considering potential confounding factors such as the addition of para-aortic lymphadenectomy, RS, and adjuvant treatment, showed that the SLN group had a lower risk of worsening oHP at six months post-surgery and lower risk of lymphedema compared to the CL group. It is possible that the results obtained from a small sample size may not be entirely reliable for drawing strong conclusions. Further studies are necessary to prevent bias.

We must consider that there are multiple external factors unrelated to oncological disease that could negatively influence overall QoL, especially in patients over 60 years of age. These factors include the

onset of new conditions such as osteoarthritis, cardiovascular diseases, fractures, or other causes that were not accounted for in these studies.

### 5.1. Strengths and weaknesses

The sample size of our study may be considered small, as it is a unicentric investigation. Consequently, strong conclusions cannot be drawn, and this issue warrants further exploration. Our study is one of the few prospective comparative studies to evaluate the impact on QoL according to lymph node staging technique in patients undergoing surgical treatment for early-stage EC. Unlike other studies (García-Pineda et al., 2023; Gonçalves et al., 2023), the sample sizes of both groups in our study are very similar, which strengthens the results. The series by Dinoi et al. (Dinoi et al., 2023) presented a fairly large and balanced sample size between both groups (101 patients in CL group and 120 in SLN group), although the study was retrospective. Additionally, we accounted for the potential bias of receiving complementary treatment after surgery. However, we used a very generic HR-QoL scale and did not consider, unlike other studies, the impact on the sexual domain. Further, we did not account for confounding factors such as the onset of new conditions unrelated to EC during the follow-up period.

## 6. Conclusions

Our study demonstrates that pelvic sentinel lymph node (SLN) biopsy in early-stage endometrial cancer patients results in better overall health perception (oHP) and healthrelated quality of life (HRQoL) compared to complete pelvic lymphadenectomy (CL). The SLN group exhibited significantly lower rates of symptomatic lymphedema and lymphocele. No significant differences were observed in intra- and postoperative complications between the SLN and CL groups. These findings support the use of SLN biopsy as a preferable staging technique to minimize morbidity and enhance quality of life in endometrial cancer survivors.

Although no significant differences were observed between patients lost to follow-up and those included in the final analysis, the possibility of attrition bias cannot be entirely excluded. This limitation should be considered when interpreting the results.

### Informed Consent Statement

Patients provided written informed consent to participate in this study.

**Institutional Review Board Statement:** The study was conducted following the Declaration of Helsinki and was approved by the local Ethics Committee of Balearic Islands, Spain (CEI-IB. Ref. IB 363 4103/20 PI).

### Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author Anna Torrent used Chat GPT only in order to improve language. After using this tool the author reviewed and edited the content as needed and take full responsibility for the content of the publication.

### CRediT authorship contribution statement

**Anna Torrent:** Writing – original draft, Validation, Supervision, Software, Methodology, Investigation, Data curation, Conceptualization. **Joana Amengual:** Writing – review & editing, Supervision. **Angela Ruiz:** Formal analysis, Data curation. **Aina Serra:** Data curation. **Laura Fuertes:** Data curation. **Catalina Maria Sampol:** Writing – review & editing, Visualization. **Mario Ruiz:** Data curation. **Jorge Rioja:** Data curation. **Pilar Roca:** Writing – review & editing, Formal analysis, Conceptualization. **Octavi Cordoba:** Writing – review &

editing, Methodology, Investigation.

### Funding

This research was not funded by any organization.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgments

We would like to thank Aina Millan statistician at IdISBa for her support, and we extend our special gratitude to all the patients who agreed to participate in this study.

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