

ORIGINAL RESEARCH

Enhanced recovery after surgery (ERAS) for laparoscopic hysterectomy in low-risk endometrial cancer: a randomized controlled trial

Laura Cánovas-López^{1,2,†}, Iryna Kozak¹, Alberto Rafael Guijarro-Campillo^{1,3,*}, Carla Castañer⁴, Luis Falcón-Araña⁴, Julian J. Areñse-Gonzalo⁵, Francisco Barceló-Valcarcel^{1,2}, Victor Lago^{6,7}, Anibal Nieto^{1,2,†}, Marisa Sánchez-Ferrer^{1,2,†}

¹Department of Gynecologic Oncology, Virgen de la Arrixaca University Clinical Hospital, 30002 Murcia, Spain

²Murciano Institute of Biomedical Research, IMIB, 3002 Murcia, Spain

³University of Valencia, 46010 Valencia, Spain

⁴Department of Anesthesiology and Resuscitation, Virgen de la Arrixaca University Clinical Hospital, 30002 Murcia, Spain

⁵Division of Preventive Medicine and Public Health, Department of Public Health Sciences, School of Medicine, University of Murcia, 30002 Murcia, Spain

⁶Department of Gynecologic Oncology, La Fe University and Polytechnic Hospital, 46026 Valencia, Spain

⁷CEU San Pablo University, 12006 Castellón, Spain

*Correspondence

alguicam@alumni.uv.es

(Alberto Rafael Guijarro-Campillo)

† These authors contributed equally.

Abstract

Background: Enhanced Recovery After Surgery (ERAS) programs aim for early recovery and reduced hospital length of stay (LOS). Their role in specific patient groups, such as those with early-stage endometrial cancer undergoing Minimally Invasive Surgery (MIS), is not well understood. **Methods:** This randomized controlled trial included low-risk patients with early-stage endometrial cancer who underwent total hysterectomy and salpingo-oophorectomy by laparoscopy. Patients were assigned to an ERAS protocol or a conventional control (CC) protocol. The primary outcome was LOS, while secondary outcomes included perioperative morbidity and quality of life (QoL). **Results:** From June 2019 to August 2021, 92 women were recruited, with 24 exclusions. Compliance with ERAS was 87.9%. ERAS patients showed significantly reduced hospitalization, with 67.6% discharged on the first postoperative day compared with 20.6% in the CC group ($p < 0.001$). Median LOS was 1 day (interquartile range (IQR) 1–2) for ERAS vs. 2 days (IQR 2–2) for CC ($p < 0.001$). No significant differences were found in postoperative complications or readmissions. However, QoL improved significantly in the ERAS group at 10 days ($p = 0.012$) and 30 days ($p < 0.001$) post-surgery, based on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). Pain scores on the Visual Analogue Scale (VAS) were also better in the ERAS group at 3 and 10 days ($p = 0.023$ and $p = 0.041$). **Conclusions:** Patients with early-stage endometrial cancer benefit from ERAS protocols, achieving lower LOS and improved QoL after MIS. **Clinical Trial Registration:** NCT06732635, retrospectively registered.

Keywords

Endometrial cancer; Quality of life; Enhanced recovery after surgery

1. Introduction

The surgical management of endometrial cancer has undergone major changes since the beginning of Minimally Invasive Surgery (MIS) in early-stage endometrial cancer [1, 2].

In addition, clinical pathways have been improved with the introduction of Enhanced Recovery After Surgery (ERAS) [3]. It has been widely accepted as an advanced approach for the management of patients undergoing colorectal and numerous other types of surgery, with standardized guidelines provided by the ERAS Society (www.erassociety.org) for each surgical procedure. The key principles of ERAS protocols include interventions implemented at three different stages: preoperative, intraoperative, and postoperative. All these interventions require close coordination among a multidisciplinary team.

Even though there are gynecological oncology guidelines

provided by ERAS Society, many of these recommendations come from evidence in colorectal surgery. Despite the positive conclusions and reported benefits of applying ERAS protocols in gynecologic oncology, several published studies emphasize the significant heterogeneity of the populations evaluated, highlighting the need for prospective designs that examine the role of ERAS programs in patients with a specific pathology who undergo a defined surgical approach [4]. To date, only three prospective randomized studies have exclusively analyzed patients with gynecologic cancers, providing a high level of scientific evidence [5–7]. To our knowledge, no studies have specifically evaluated ERAS pathways in endometrial cancer treated by laparoscopy.

This study, therefore, aims to evaluate whether ERAS pathways are beneficial for patients with endometrial cancer, particularly those with low-risk early-stage disease undergoing la-

paroscopic surgery. Length of stay (LOS), perioperative morbidity and mortality, and perioperative quality of life (QoL) were analyzed by comparing patients managed under ERAS pathways with those treated using conventional protocols.

2. Methods

2.1 Design

This study was a prospective, randomized clinical trial that enrolled patients diagnosed with low-risk endometrial carcinoma on an IA stage as indicated by International Federation of Gynecology and Obstetrics (FIGO 2009) staging guidelines after clinical examination, and histopathological verification. The study was carried out at the Virgen de la Arrixaca University Clinical Hospital in Murcia between June 2019 and August 2021. The study was approved by the Ethical and Clinical Research Committee of the sponsoring center (2019-3-8-HCUVA, **Supplementary material 1**), in accordance with the requirements of Law 14/2007 of 03 July on Biomedical Research and the Declaration of Helsinki. Patient recruitment covered the period from June 2019 to August 2021. Patients with endometrial carcinoma (grade 1 or 2) underwent pretherapeutic clinical staging based on physical examination, levels of tumor marker carbohydrate antigen (CA) 125, and pelvic ultrasonography. An expert sonographer routinely performed the local evaluation of the disease in our center, determining the level of myometrial invasion. Exclusion criteria for the study included active ischemic heart disease, advanced cirrhosis, severe psychiatric disease, an American Society of Anesthesiologists scale (ASA) IV physical status classification, or urgent surgery due to critical complications. Patients who experienced upstaging after the surgical specimen evaluation (tumor grade >2 or FIGO stage >IA) were also excluded.

2.2 Randomization

At the time of study inclusion, patients were randomized in a 1:1 ratio to either the experimental (ERAS) or the conventional control (CC) group using a simple blinded randomization system conducted by an independent committee from the Instituto Murciano de Investigación Biosanitaria (IMIB). All patients provided informed consent and were fully briefed on the study (**Supplementary material 2**). Each individual received a unique identifier for data correlation, ensuring confidentiality at all times. Data were collected prospectively from the initial visit up to the final postoperative check-up, 30 days after hospital discharge.

2.3 Criteria selection

Patients with low-risk endometrioid carcinoma (grade 1 or 2 and superficial myometrial invasion <50%), as defined by the European Society of Gynecological Oncology (ESGO) recommendations in place at the time of the study design, were recruited. The standard surgery was based on hysterectomy with double bilateral salpingo-oophorectomy without vaginal cuff [8].

The primary objective of this study was to determine

whether there are differences in LOS between Conventional and ERAS protocols groups. Comparing perioperative morbidity, perioperative QoL and postoperative pain measured on a visual analog scale (VAS).

Postoperative complications were recorded based on their type and severity according to the Clavien-Dindo classification [9]. The QoL was measured using the validated European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) [10], which was carried out preoperatively (1 month before surgery), and at 3, 10, and 30 days after surgery.

2.4 Conventional control vs. ERAS protocol

An ERAS protocol was developed by a multidisciplinary team of gynaecologists, oncologists, anaesthesiologists, endocrinologists, and nurses based on updated recommendations of the ERAS Society 2019 [11]. As established by the ERAS Society, the items included preoperative, intraoperative, and postoperative periods **Supplementary Table 1**. Patients in the CC group were managed based on traditional behaviors from the ERAS protocol group as shown in **Supplementary Table 2**. The ERAS protocols included strategies such as same-day admission, preoperative carbohydrate loading, multimodal analgesia, early mobilization at 6 hours postoperatively, and respiratory physiotherapy. This protocol emphasizes screening for anemia and diabetes, multimodal analgesia with minimal opioid use, and self-administration of low molecular weight heparin at home. In contrast, the conventional care protocol involves admission the day before surgery, standard opioid-based analgesia, and delayed mobilization until 24 hours postoperatively.

The laparoscopic hysterectomy and salpingo-oophorectomy were standardized. A pneumoperitoneum was created by Veress needle (Mock Medical, Milford, MA, USA). 10 mm umbilical trocar was used for optics and three 5 mm trocars were inserted under direct vision. A team of two specialists alternating as surgeon and assistant performed all the procedures. All patients were discharged with the same criteria: normal vital signs, acceptable pain with prescribed painkillers, and ability to eat without nausea.

Follow-up was performed by telephone monitoring by the nurse case manager on days 3 and 10 after the intervention. This follow-up included: pain using the VAS (**Supplementary Fig. 1**), EORTC QLQ-C30 questionnaire, complications rated with Clavien-Dindo classification, emergency consultations and re-admissions. The QoL of the patients assessed using the EORTC QLQ-C30 questionnaire contains 2 parts. The first consists of 28 questions, to which the patient must answer from 1 to 4 indicating whether she has presented little/a lot of the signs/symptoms in question during the last week. Therefore, the score for this section ranges from a minimum of 28 points to a maximum of 112 points, with higher scores indicating worse QoL. The second part consists of two questions. In the first, patients rate their overall health during the past week on a scale from 1 to 7, with higher scores indicating better health. The second question uses the same scale to assess their overall QoL during the past week. Therefore, in this second part, the higher the score, the better the perception of QoL, which can

vary from 2 to 14 points. An in-person follow-up visit 30 days after the intervention was also included in the study and was conducted by both the gynecologic oncologist and the nurse case manager, as described above.

2.5 Statistics

A sample size of 62 women (31 per group, assuming a 1:1 allocation ratio) was estimated based on a review of the LOS of patients operated on for endometrial cancer between 2013 and 2015. We aimed to detect a minimum difference of 1 day in LOS between the intervention and control groups. Thus, with a significance level of 95% and a power of 80%, we estimated a minimum sample of 31 patients per group. If we assume a loss of 10%, the final sample size would be 34 patients per group.

The statistical analysis was carried out with the Statistical Package for Social Sciences (SPSS) program (version 25; IBM Corp., Armonk, NY, USA). The quantitative variables with normal distribution were reported as mean and standard deviation, and those that did not, as median and the interquartile range (IQR). Quantitative analysis to explore differences between the 2 groups was carried out using *t*-test for normality and Mann-Whitney U test for abnormal distribution. Chi-square and Fisher tests were used for categorical variables. LOS was assessed as a quantitative variable and also as a dichotomous variable, depending on whether the patient was able to go home on the first postoperative day, or had to be hospitalized for 2 days or more. Data were analyzed using IBM SPSS software (version 25; IBM Corp., Armonk, NY, USA), and the differences were considered statistically significant at

p -values < 0.05 .

3. Results

Between June 2019 and August 2021, 92 patients were recruited to the study and randomized to ERAS or CC group. From those patients who met the inclusion criteria, 12 were not included because they refused to participate in the study. Another 12 patients were not recruited because they were diagnosed and treated during February, March, April, and May 2020. Given the situation of the COVID-19 pandemic, recruitment was suspended to avoid exposing study patients to additional risk (Fig. 1).

Both groups were similar regarding demographic and clinical data except for previous surgeries more common in the ERAS group (Table 1).

A total of 23 patients in the intervention group (67.6%) and 7 patients in the control group (20.6%) were discharged from the hospital on the first postoperative day ($p < 0.001$) (Table 2). The median for “admissions days” was 1 (IQR 1–2) vs. 2 (IQR 2–2), $p < 0.001$, for ERAS and CC group, respectively (Table 2).

The type of postoperative complications were divided into 3 groups: digestive, infectious, and others. Consultations at the Emergency Department after hospital discharge were also monitored. No significant differences were found between the groups, either overall or when complications were classified by severity according to the Clavien-Dindo system (Table 3). The complications by stages and more are described in **Supplementary Table 3**.

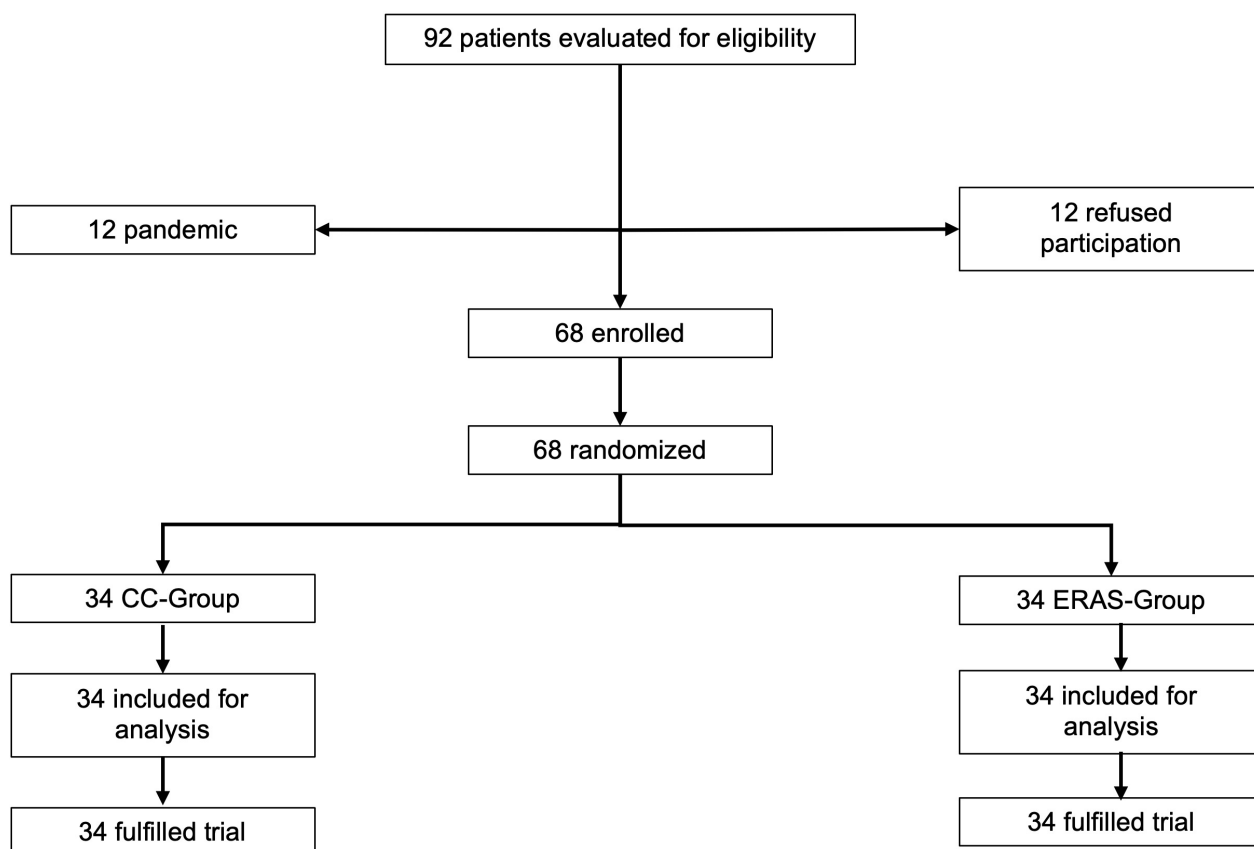


FIGURE 1. Flow-chart trial. CC: Conventional Control; ERAS: Enhanced Recovery After Surgery.

TABLE 1. Demographic and clinicopathological characteristics.

	ERAS	CC	Total	<i>p</i>
Mean Age (yr) (SD)	58.15 (10.39)	60 (2.13)		0.5
Race, n (%)				
Caucasian/White	31 (91.2)	34 (100)	65 (95.6)	0.239
American/Red	3 (8.8)	0	3 (4.4)	
Pregnancies, n (%)				
Nulliparous	2 (5.9)	6 (17.6)	8 (11.8)	0.259
≥1 pregnancy	32 (94.1)	28 (82.4)	60 (88.2)	
Menarche, median years (IQR)	12.71 (12.00–14.00)	12.09 (11.00–13.00)		0.123
Menopause, n (%)				
Yes	28 (82.4)	24 (70.6)	52 (76.5)	0.067
No	6 (17.6)	10 (29.4)	16 (23.5)	
Median Menopausal Years (IQR)	10.93 (3.25–16.25)	14.75 (5.5–23.75)		0.089
Weight (kg), mean (SD)	78.69 (14.69)	79.97 (17.04)		0.741
Height (cm), mean (SD)	157.91 (5.32)	160.26 (7.17)		0.129
BMI, n (%)				
18.5–24.99	5 (14.7)	6 (17.6)	11 (16.2)	0.98
25.00–29.99	8 (23.5)	8 (23.5)	16 (23.5)	
30.00–34.99	11 (32.4)	9 (26.5)	20 (29.4)	
35.00–39.99	8 (23.5)	9 (26.5)	17 (25)	
≥40.00	2 (5.9)	2 (5.9)	4 (5.9)	
History of previous abdominal surgery, n (%)	21 (61.8)	11 (32.4)	32 (47)	0.01
Diabetes, n (%)	6 (17.6)	7 (20.6)	13 (19.1)	0.75
History of hormone replacement therapy (HRT), n (%)	2 (5.9)	2 (5.9)	4 (5.9)	1.00
History of use of OCPs, n (%)	14 (41.2)	18 (52.9)	32 (47)	0.33
History of IUD use, n (%)	1 (2.9)	3 (8.8%)	4 (5.9)	0.61
History of radio/chemotherapy, n (%)	0	5 (14.7)	5 (7.4)	0.05
Smoking, n (%)	6 (17.6)	8 (23.5)	14 (20.6)	0.54
No. of cigarettes/day, median (IQR)	15.17 (5.00–20.25)	10.38 (6.25–13.75)		0.32
Alcohol Habit, median (IQR)	0	0	0 (100.0)	
Degree of differentiation (Adenocarcinoma), n (%)				
G1	25 (86.2)	23 (92.0)	48 (88.9)	0.63
G2	1 (3.4)	0	1 (1.9)	
G3	1 (3.4)	1 (4)	2 (3.7)	
Unknown	2 (6.9)	1 (4)	3 (5.6)	

ERAS: Enhanced Recovery After Surgery; CC: conventional control; SD: standard deviation; IQR: interquartile range; BMI: body mass index; OCPs: oral contraceptives; IUD: intrauterine device.

TABLE 2. LOS analysis according to the day of hospital discharge and to the time of hospital admission.

	ERAS	CC	<i>p</i>
Day of discharge, n (%)			
1st POD	23 (67.6%)	7 (20.6%)	<0.001
≥2nd POD	11 (32.4%)	27 (79.4%)	
Mean, d (SD)	1.47 (0.83)	2.06 (0.85)	<0.001*
Median, d (IQR)	1 (1–2)	2 (2–2)	<0.001*

SD: standard deviation; IQR: interquartile range; POD: Post-Operative Day; ERAS: Enhanced Recovery After Surgery; CC: conventional control.

*Mann-Whitney U-test, *p* values adjusted for ties.

TABLE 3. Postoperative complications and re-admissions.

	ERAS	CC	<i>p</i>
Digestive complications, n (%)	16 (47)	12 (35.3)	0.460
Infectious complications, n (%)	8 (23.5)	8 (23.5)	1.000
Other complications, n (%)	22 (64.7)	19 (55.9)	0.621
Emergency Consultation, n (%)	10 (29.4)	8 (23.5)	0.784
Grade, n (%)			
No complications	12 (35.3)	15 (44.1)	
I	18 (52.9)	14 (41.2)	
II	2 (5.9)	4 (11.8)	0.64
IIIa	1 (2.9)	1 (2.9)	
IIIb	1 (2.9)	0 (0)	
Re-admissions, n (%)	2 (5.9)	5 (14.7)	0.427

ERAS: Enhanced Recovery After Surgery; CC: conventional control.

No differences were found in re-admissions: two patients in ERAS (5.9%) vs. five patients in CC group (14.7%) ($p = 0.427$). Out of the two patients in the intervention group, one was due to infection of the vaginal cuff and the second patient was readmitted due to respiratory decompensation in the context of her underlying heart failure. In the control group, one of them for vaginal cuff bleeding, which was controlled without the need for any invasive procedure. Two patients were admitted for urinary fever, one due paralytic ileus, and another because of an infected collection and hemoperitoneum. This last patient had to be reoperated under general anesthesia.

All women completed the questionnaires. As aforementioned, the QoL survey (EORTC QLQ-C30) was carried out at 4 different times: preoperatively (1 month before surgery), and at 3, 10, and 30 days after surgery. At 3 and 10 days after surgery, there were no differences in the median QoL global scores between the groups ($p = 0.466$ and 0.058). No differences were found in the scores for day 3 ($p = 0.858$); however, a significant improvement on day 10 was observed in the ERAS group ($p = 0.012$) (Table 4). It was on day 30 of the postoperative period where clear improvements in QoL differences were found in favor of the ERAS group for both scores ($p < 0.001$). Similarly, throughout the follow-up, the scores within each group improved (Fig. 2).

On the first postoperative day, there was a higher score on the VAS pain scale for the ERAS group, which was not significant (ERAS 2.62 (IQR 1–3.5) vs. CC 2.41 (IQR 1–3), $p = 0.693$). However, pain was significantly lower for ERAS groups at 3 and 10 postoperative days (2.15 (IQR 0.75–3) vs. 3.65 (IQR 1–5.2), $p = 0.023$ and 2.09 (0–4) vs. 3.09 (1–5), $p = 0.041$, respectively) (Table 4).

Compliance with the ERAS protocol, which was defined as the average compliance rate for each of the measures, was 87.9% (Supplementary Table 1). Significant differences were observed in the following measures shared between both perioperative management protocols: preoperative fasting to liquids (ERAS 2.72 h (IQR 8–12) vs. CC 10.82 h (IQR 8–12),

$p < 0.001$), use of compression stockings (ERAS 100% vs. CC 8.8%, $p < 0.001$), initiation of tolerance to liquids (ERAS 6.65 h (IQR 6–6) vs. CC 20.94 h (IQR 20–24), $p < 0.001$) and solids (ERAS 19.03 h (IQR 12–24) vs. CC 24 h (IQR 24–24), $p < 0.001$), and at the beginning of mobilization (23.41 h (24–24) vs. 24.71 h (24–24), $p = 0.045$).

4. Discussion

To the best of our knowledge, this is the first RCT comparing ERAS and conventional management in a specific group of patients with early-stage endometrial cancer. We demonstrated that ERAS protocol during the perioperative management of laparoscopic hysterectomy and salpingo-oophorectomy performed in low-risk endometrial cancer patients showed benefits in terms of a decrease in LOS and an improvement in QoL of these patients. Furthermore, ERAS did not increase the rate of re-admissions, complications, and postoperative pain.

Previous studies have demonstrated that the ERAS protocol improves outcomes in different settings of patients with gynecologic cancers [4]. Only a few have analyzed homogeneous populations focused on specific cancers [12, 13] and only 3 of them are RCTs; one in ovarian cancer, another in cervical cancer, and the last one was a non-specific cancer [6, 14, 15]. There are also results in favor of ERAS protocols in laparoscopic [16] vaginal [17] and abdominal hysterectomy for benign disease [18]. With the aim of studying the real benefits of ERAS in patients with gynecological-oncological pathology, O'Neill *et al.* [4], published a meta-analysis showing the great heterogeneity of the patients, with a great variability expected in morbidity as well as the different types of surgery and approaches. Our study is the only one so far that focuses on a very specific group of early-stage endometrial cancer with a minimally invasive approach. Our results could be comparable to those of other RCTs where patients with hysterectomy due to benign causes are compared [18, 19]. As well as that, it could be compared with the study by Chen *et*

TABLE 4. QoL (EORTC QLQ-C30) evolution and pain (VAS scale) between groups.

Questionnaire/scale	Study group	Control group	Differences		p value
EORTC QLQ-C30	ERAS	CC	Post-operative vs. baseline ERAS	CC	p*
Preoperative, median (IQR)					
Global	36.32 (32.00–40.25)	43.09 (33.0–52.0)	NA		
Questions	11.65 (12.0–14.0)	9.97 (9.0–11.5)			
Day 3 median (IQR)					
Global	36.53 (32.0–41.0)	42.68 (33.75–47.50)	0.21	0.41	0.466
Questions	11.91 (10.75–14.0)	10.15 (9.0–12.0)	0.26	0.18	0.858
Day 10 median (IQR)					
Global	33.62 (30.0–36.25)	41.59 (31.75–44.25)	2.7	1.5	0.058
Questions	12.44 (11.0–14.0)	10.26 (9.75–12.0)	0.79	0.29	0.012
Day 30 median (IQR)					
Global	31.41 (29.0–32.25)	37.56 (29.75–41.50)	4.91	5.53	<0.001
Questions	12.91 (12.0–14.0)	11.74 (11.0–14.0)	1.26	1.77	<0.001
VAS scale	ERAS	CC		p	
Immediate postoperative median (IQR)	2.62 (1.0–3.5)	2.41 (1.0–3.0)		0.693	
Day 3 median (IQR)	2.15 (0.75–3.0)	3.65 (1.0–5.2)		0.023	
Day 10 median (IQR)	2.09 (0.0–4.0)	3.09 (1.0–5.0)		0.041	
Day 30 median (IQR)	1.38 (0.0–2.0)	1.62 (0.0–2.0)		0.566	

IQR: interquartile range; CC: Conventional Control; ERAS: Enhanced Recovery After Surgery; VAS: visual analog scale; NA: not applicable; EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

**Mann-Whitney U-test, p values adjusted for ties.*

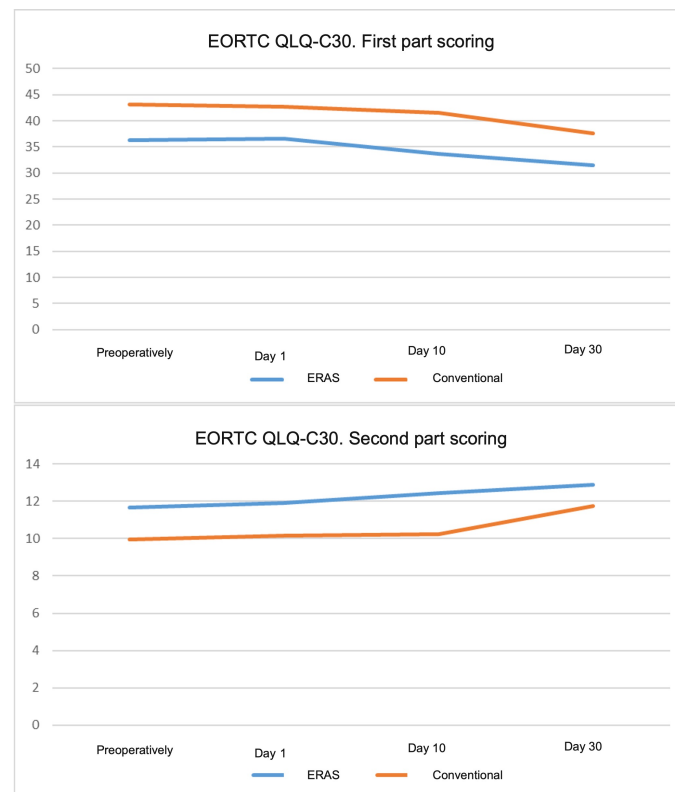


FIGURE 2. Evolutionary comparison of the two parts of the EORTC QLQ-C30 quality of life questionnaire. ERAS: Enhanced Recovery After Surgery; EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

al. [14], on cervical cancer, where a reduction in LOS was obtained with no differences in the rates of complications or re-admission. However, the aforementioned patients are far from the endometrial cancer patients, as it should be noted that they are oncological patients, characteristically older, and with higher body mass index (BMI). The average age of our sample was 59 years, almost 10 years older than the highest average age of the previously discussed studies. The mean BMI of our sample was 34 with up to 25% of the patients >35, far from the mean BMI that in none of the aforementioned studies reaches 30. The benefits of multimodal rehabilitation increase as the complexity of surgery grows [20]. Our study shows that, in addition to our population and despite a higher expected morbidity, comparable beneficial ERAS results in LOS reduction were found.

There has been some skepticism regarding the additional benefit of ERAS when applied to MIS. One might think that since the benefits of ERAS have been demonstrated to a greater extent, as the complexity of the surgery increases and the more aggressive the approach is, there is little room for improvement in MIS. MIS, whether robotic or laparoscopic, favors many of the ERAS interventions, such as normothermia, early mobilization or reduction of paralytic ileus. Aubrey *et al.* [21], showed in a recent systematic review that the implementation of ERAS in minimally invasive gynecologic oncology surgery was associated with increased rates of same-day discharge (SDD), decreased opioid use, improved satisfaction, and cost savings. Most studies did not detail the specific surgical procedures and included a variety of different gynecologic cancer diagnoses. One of the most beneficial results showed by ERAS in MIS is the improvement in the rate of SDD [22]. There is still a lot of reluctance in relation to these early discharges, especially due to the lack of unanimous criteria based on strong evidence, among which is the BMI as an exclusion criteria [23]. The growing evidence supporting the benefits of SDD encourages the consideration of implementing these measures in carefully selected populations, similar to those included in our trial.

A few studies have evaluated patient satisfaction and QoL as the main objective in association with the ERAS protocol after colorectal surgery [24]. A recent meta-analysis presented an improved QoL after simple minimally invasive hysterectomy compared with abdominal hysterectomy for benign disease and endometrial cancer, but not within ERAS programs [25]. Ferrari *et al.* [26] have been the only ones who designed a study to specifically assess QoL in patients after surgery for initial endometrial cancer. This investigation demonstrated benefits in the ERAS group for the physical functioning, role-physical, and social functioning domains. It is true that not all patients underwent MIS, and the LOS between both groups was higher than in the two groups in our study (median LOS 5 vs. 3 days for conventional and ERAS group). Our results indicate that ERAS provides additional benefits to the already improved QoL observed in patients undergoing MIS.

Previous studies on colorectal surgery have found that at least 70% of the ERAS protocol must be applied to be effective [27]. We obtained an overall rate of 87.9% for all patients. It is certainly remarkable that early mobilization was not achieved in any of the patients in the ERAS group. Although the entire

multidisciplinary group that participated in the study was instructed, it should not be forgotten that this was the first cluster of patients within the Gynecology Department where these measures were applied. In a recent survey of 116 accredited individuals with the European Society of Gynecologic Oncology, early mobilization was carried out in only 55% of them [28]. Despite the critical importance of early mobilization in the ERAS protocol, which aims to avoid ileus, promote early tolerance, and facilitate early discharge, it was not achieved in any patients in our ERAS group. The reasons for this noncompliance include a lack of training and communication of nursing staff. This challenge may have limited the reduction in LOS and negatively affected postoperative QoL. However, positive results were still obtained, suggesting that other ERAS interventions contributed significantly to these outcomes. In light of these results, measures have been implemented to rectify this aspect, primarily through the establishment of a dedicated nursing team and enhanced communication with the medical staff. Consequently, greater benefits are anticipated for patients managed within the program.

In gynecological laparoscopic surgery under ERAS protocol, Opioid Free Anesthesia (OFA) technique is non-inferior to Opioid Anesthesia (OA) technique in analgesic effect and intraoperative anesthesia stability. Although awakening and orientation recovery times were prolonged compared with OA, OFA had a lower incidence of postoperative nausea or vomiting and improved postoperative sleep quality [29]. Our results show that despite not using opioid analgesia during the stay in the Hospitalization Ward, this was not the case in the Resuscitation Unit. It is a measure agreed upon with the Anesthesia Unit during the protocol elaboration, which is considered a small quantity to cause the postoperative complications expected by the administration of opioids. In addition, our study showed that the benefits in postoperative pain were not evident immediately after surgery, but became apparent from postoperative day 3 onwards. Individual differences in pain perception and response to analgesics may also influence these results. Factors such as psychological status, history of preoperative pain, and the influence of early mobilization will be examined in further research.

4.1 Strengths and weaknesses

The strengths of our study were the randomized nature of the trial and the standardized protocols applied to a very specific group of patients. There are, however, some limitations to our study. The sample size, while sufficient for detecting differences in LOS, may limit the power for secondary outcomes, such as complications and QoL sub-domains. This should be acknowledged when interpreting the results. A small cohort of patients was selected with a pre-established design and carried out in a single institution. Recruitment took more time due to the COVID-19 pandemic. In addition, the reluctance to adopt the ERAS protocol may have been influenced by the unfamiliarity of the responsible clinician with the protocol and its principles at the time of recruitment. The delay in presenting the results was due to the need for thorough data collection and analysis, which prolonged the compilation and interpretation process. Despite this delay, we believe the

findings are significant contributions to the field.

4.2 Implications for future practice and research

It remains to be determined which patients could benefit from the inclusion of measures in the ERAS protocols such as SDD. So far, one of the exclusion criteria is BMI, without being able to clearly determine where the cut-off point could be located. In addition, the arrival of robotic surgery in gynecology is becoming more and more widespread. Retrospective studies show that robotic surgery is not inferior to other approaches and may have advantages when compared to laparoscopy in obese patients [30]. Robotic approach could even improve the outcomes of ERAS protocols in patients with endometrial cancer with high BMIs.

5. Conclusions

In summary, there are benefits in ERAS implementation for early-stage endometrial cancer patients treated by laparoscopy, revealing a shorter LOS due to earlier recovery and QoL improvement without increasing postoperative complications or re-admissions. This study provides evidence for considering ERAS in this specific group of patients.

AVAILABILITY OF DATA AND MATERIALS

Data is available from the authors upon reasonable request.

AUTHOR CONTRIBUTIONS

LCL and IK—have collected the data. LCL, IK, ARGC and JJAG—have made the power calculations and statistical analyses. LFA and CC—are responsible for the anesthesiology protocol. ARGC—has written the manuscript. FBV, AN, MSF, LCL and IK—designed and promoted the study. VL—helped with improvements in the design phase. AN and MSF—oversaw all phases of the process. All authors participated in some modifications of the manuscript. All authors meet the ICMJE criteria for authorship. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ethical and Clinical Research Committee of the sponsoring center (2019-3-8-HCUVA, **Supplementary material 1**), in accordance with the requirements of Law 14/2007 of 3 July on Biomedical Research and the Declaration of Helsinki. All patients provided informed consent and were fully briefed on the study (**Supplementary material 2**). Full trial protocol can be accessed at [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT06732635) (NCT06732635).

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at <https://oss.ejgo.net/files/article/2110266049326661632/attachment/Supplementary%20material.zip>.

REFERENCES

- [1] Tankou J, Pollack LM, Wilson E, Kuo I, Wang M, Eckhouse SR, *et al.* Cost-effectiveness of combined minimally invasive hysterectomy and bariatric surgery in women with morbid obesity and endometrial hyperplasia or early-stage endometrial cancer. *Journal of Minimally Invasive Gynecology*. 2026; 33: 283–290.
- [2] Cucinella G, Di Donna MC, Solazzo MC, Ronsini C, Scaffa C, Chiantera V. Robotic surgery in endometrial cancer using robot da Vinci® SP. *Annals of Surgical Oncology*. 2026; 33: 1134.
- [3] Nelson G, Fotopoulou C, Taylor J, Glaser G, Bakkum-Gamez J, Meyer LA, *et al.* Enhanced recovery after surgery (ERAS®) society guidelines for gynecologic oncology: addressing implementation challenges—2023 update. *Gynecologic Oncology*. 2023; 173: 58–67.
- [4] O'Neill AM, Calpin GG, Norris L, Beirne JP. The impact of enhanced recovery after gynaecological surgery: a systematic review and meta-analysis. *Gynecologic Oncology*. 2023; 168: 8–16.
- [5] Yi HC, Ibrahim Z, Abu Zaid Z, Mat Daud Z, Md Yusop NB, Omar J, *et al.* Impact of enhanced recovery after surgery with preoperative whey protein-infused carbohydrate loading and postoperative early oral feeding among surgical gynecologic cancer patients: an open-labelled randomized controlled trial. *Nutrients*. 2020; 12: 264.
- [6] Sánchez-Iglesias JL, Carbonell-Socias M, Pérez-Benavente MA, Monreal Clua S, Manrique-Muñoz S, García Gorris M, *et al.* PROFAST: a randomised trial implementing enhanced recovery after surgery for highcomplexity advanced ovarian cancer surgery. *European Journal of Cancer*. 2020; 136: 149–158.
- [7] Chiewhatpong P, Charoenkwan K, Smithiseth K, Lapisatepun W, Lapisatepun P, Phimphilai M, *et al.* Effectiveness of enhanced recovery after surgery protocol in open gynecologic oncology surgery: a randomized controlled trial. *International Journal of Gynecology & Obstetrics*. 2022; 159: 568–576.
- [8] Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, *et al.* ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up. *Radiotherapy and Oncology*. 2015; 117: 559–581.
- [9] Dindo D, Demartines N, Clavien P. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals of Surgery*. 2004; 240: 205–213.
- [10] Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, *et al.* The European organization for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*. 1993; 85: 365–376.
- [11] Nelson G, Bakkum-Gamez J, Kalogera E, Glaser G, Altman A, Meyer LA, *et al.* Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery after Surgery (ERAS) Society recommendations—2019 update. *International Journal of Gynecological Cancer*. 2019; 29: 651–668.
- [12] Mateshaytis J, Brawner M, Steed H, Pin S. Improving the rate of same-day discharge in gynecologic oncology patients with endometrial cancer undergoing minimally invasive robotic surgery: a quality improvement

- initiative. *Journal of Minimally Invasive Gynecology*. 2022; 29: 1184–1193.
- [13] Miguet C, Jauffret C, Zemmour C, Boher JM, Sabiani L, Houvenaeghel G, *et al*. Enhanced recovery after surgery and endometrial cancers: results from an initial experience focused on elderly patients. *Cancers*. 2023; 15: 3244.
- [14] Chen L, Yuan Q, Li J. Effect of enhanced recovery after surgery on curative effect and prognosis of patients undergoing laparoscopic hysterectomy for cervical cancer. *International Journal of Clinical and Experimental Medicine*. 2020; 13: 2613–2620.
- [15] Ferrari F, Forte S, Sbalzer N, Zizioli V, Mauri M, Maggi C, *et al*. Validation of an enhanced recovery after surgery protocol in gynecologic surgery: an Italian randomized study. *American Journal of Obstetrics and Gynecology*. 2020; 223: 543.e1–543.e14.
- [16] Minig L, Chuang L, Patrono MG, Fernandez-Chereguini M, Cárdenas-Rebollo JM, Biffi R. Clinical outcomes after fast-track care in women undergoing laparoscopic hysterectomy. *International Journal of Gynecology & Obstetrics*. 2015; 131: 301–304.
- [17] Relph S, Bell A, Sivashanmugarajan V, Munro K, Chigwidden K, Lloyd S, *et al*. Cost effectiveness of enhanced recovery after surgery programme for vaginal hysterectomy: a comparison of pre and post-implementation expenditures. *The International Journal of Health Planning and Management*. 2014; 29: 399–406.
- [18] Kilpiö O, Härkki PSM, Mentula MJ, Väänänen A, Pakarinen PI. Recovery after enhanced versus conventional care laparoscopic hysterectomy performed in the afternoon: a randomized controlled trial. *International Journal of Gynecology & Obstetrics*. 2020; 151: 392–398.
- [19] Bahadur A, Mallick BK, Heda A, Pathak A, Heda S, Mundhra R. Comparison of the outcomes of enhanced recovery after surgery and traditional recovery pathway in robotic hysterectomy for benign indications: a randomized controlled trial. *Journal of Minimally Invasive Gynecology*. 2024; 31: 601–606.
- [20] Wijk L, Udumyan R, Pache B, Altman AD, Williams LL, Elias KM, *et al*. International validation of enhanced recovery after surgery society guidelines on enhanced recovery for gynecologic surgery. *American Journal of Obstetrics and Gynecology*. 2019; 221: 237.e1–237.e11.
- [21] Aubrey C, Nelson G. Enhanced recovery after surgery (ERAS) for minimally invasive gynecologic oncology surgery: a review. *Current Oncology*. 2023; 30: 9357–9366.
- [22] Kim SR, Laframboise S, Nelson G, McCluskey SA, Avery L, Kujbid N, *et al*. Enhanced recovery after minimally invasive gynecologic oncology surgery to improve same day discharge: a quality improvement project. *International Journal of Gynecological Cancer*. 2022; 32: 457–465.
- [23] Brancazio SN, Lehman A, Kemp EV, Brown J, Crane EK, Tait DL, *et al*. Factors associated with same day discharge after laparoscopic surgery in gynecologic oncology. *Journal of Minimally Invasive Gynecology*. 2022; 29: 114–118.
- [24] Li D, Jensen C. Patient satisfaction and quality of life with enhanced recovery protocols. *Clinics in Colon and Rectal Surgery*. 2019; 32: 138–144.
- [25] Bartels HC, Rogers AC, Janda M, Obermair A, Brennan DJ. Quality of life following minimally invasive hysterectomy compared to abdominal hysterectomy: a meta-analysis. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2020; 252: 206–212.
- [26] Ferrari F, Soleymani Majd H, Giannini A, Favilli A, Laganà AS, Gozzini E, *et al*. Health-related quality of life after hysterectomy for endometrial cancer: the impact of enhanced recovery after surgery shifting paradigm. *Gynecologic and Obstetric Investigation*. 2024; 89: 304–310.
- [27] Gustafsson UO, Hausel J, Thorell A, Ljungqvist O, Soop M, Nygren J; Enhanced Recovery After Surgery Study Group. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Archives of Surgery*. 2011; 146: 571–577.
- [28] Gómez-Hidalgo NR, Pletnev A, Razumova Z, Bizzarri N, Selcuk I, Theofanakis C, *et al*. European Enhanced Recovery After Surgery (ERAS) gynecologic oncology survey: status of ERAS protocol implementation across Europe. *International Journal of Gynecology & Obstetrics*. 2023; 160: 306–312.
- [29] Chen L, He W, Liu X, Lv F, Li Y. Application of opioid-free general anesthesia for gynecological laparoscopic surgery under ERAS protocol: a non-inferiority randomized controlled trial. *BMC Anesthesiology*. 2023; 23: 34.
- [30] Corrado G, Vizza E, Cela V, Mereu L, Bogliolo S, Legge F, *et al*. Laparoscopic versus robotic hysterectomy in obese and extremely obese patients with endometrial cancer: a multi-institutional analysis. *European Journal of Surgical Oncology*. 2018; 44: 1935–1941.

How to cite this article: Laura Cánovas-López, Iryna Kozak, Alberto Rafael Guijarro-Campillo, Carla Castañer, Luis Falcón-Araña, Julian J. Arenc-Gonzalo, Francisco Barceló-Valcarcel, Victor Lago, Anibal Nieto, Marisa Sánchez-Ferrer. Enhanced recovery after surgery (ERAS) for laparoscopic hysterectomy in low-risk endometrial cancer: a randomized controlled trial. *European Journal of Gynaecological Oncology*. 2026; 47(3): 84-92. doi: 10.22514/ejgo.2026.030.