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# Prospective evaluation of an enhanced recovery after surgery (ERAS) pathway in a Norwegian cohort of patients with suspected or advanced ovarian cancer

Kristina Lindemann ,[1,2] Andreas Kleppe ,[3,4] Brynhildur Eyjólfsdóttir,[1] Svana Heimisdottir Danbolt,[1] Yun Yong Wang,[1] Anne Gjertine Heli-Haugestøl,[5] Sara L Walcott,[5] Odd Mjåland,[6] Gerd-Anita Navestad,[1] Silje Hermanrud,[1] Knut Erling Juul-Hansen,[7] Ulf Kongsgaard[2,7]

For numbered affiliations see end of article.

**Correspondence to**
Prof. Dr. Kristina Lindemann, Department of Gynecological Oncology, Oslo University Hospital, Oslo 0424, Norway; klinde@ous-hf.no

Received 6 February 2023
Accepted 18 May 2023
Published Online First 14 July 2023

► http://dx.doi.org/10.1136/ijgc-2023-004356



**To cite:** Lindemann K, Kleppe A, Eyjólfsdóttir B, *et al. Int J Gynecol Cancer* 2023;**33**:1279–1286.

## ABSTRACT

**Objective** This prospective cohort study evaluated the introduction of an enhanced recovery after surgery (ERAS) pathway in a tertiary gynecologic oncology referral center. Compliance and clinical outcomes were studied in two separate surgical cohorts.

**Methods** Patients undergoing laparotomy for suspected or verified advanced ovarian cancer at Oslo University Hospital were prospectively included in a pre- and post-implementation cohort. A priori, patients were stratified into: cohort 1, patients planned for surgery of advanced disease; and cohort 2, patients undergoing surgery for suspicious pelvic tumor. Baseline characteristics, adherence to the pathway, and clinical outcomes were assessed.

**Results** Of the 439 included patients, 235 (54%) underwent surgery for advanced ovarian cancer in cohort 1 and 204 (46%) in cohort 2. In cohort 1, 53% of the patients underwent surgery with an intermediate/high Aletti complexity score. Post-ERAS, median fasting times for solids (13.1 hours post-ERAS vs 16.0 hours pre-ERAS, p<0.001) and fluids (3.7 hours post-ERAS vs 11.0 hours pre-ERAS, p<0.001) were significantly reduced. Peri-operative fluid management varied less and was reduced from median 15.8 mL/kg/hour (IQR 10.8–22.5) to 11.5 mL/kg/hour (IQR 9.0–15.4) (p<0.001). In cohort 2 only there was a statistically significant reduction in length of stay (mean (SD) 4.3±1.5 post-ERAS vs 4.6±1.2 pre-ERAS, p=0.026). Despite stable readmission rates, there were significantly more serious complications reported in cohort 1 post-ERAS.

**Conclusions** ERAS increased adherence to current standards in peri-operative management with significant reduction in fasting times for both solids and fluids, and peri-operative fluid administration. Length of stay was reduced in patients with suspicious pelvic tumor. Despite serious complications being common in patients with advanced disease undergoing debulking surgery, a causal relationship with the ERAS protocol could not be established. Implementing ERAS and continuous performance auditing are crucial to advancing peri-operative care of patients with ovarian cancer.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is increasing implementation of enhanced recovery after surgery (ERAS) protocols in gynecological cancer management, but studies reporting on the clinical benefit of ERAS in patients with ovarian cancer are heterogenous and of varying quality.

### WHAT THIS STUDY ADDS

⇒ This large prospective study adds disease-specific evidence on the feasibility of ERAS protocols, including patients with advanced disease. ERAS increased adherence to evidence-based guidelines of peri-operative management and harmonized practice, but length of stay was only shortened for the cohort of patients with suspicious pelvic tumor.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study highlights the need for continuous performance audits, quality improvement work and further research on optimization of ERAS and prehabilitation programs. Additional effort should be made to explore evidence of bundled interventions such as ERAS.

## INTRODUCTION

Enhanced recovery after surgery (ERAS) pathways are care interventions aiming at early recovery through surgical stress-reduction and maintenance of normal physiology.[1] ERAS was initially introduced in colorectal surgery, but has subsequently been widely implemented in most surgical disciplines.[2] Updated ERAS guidelines for the management of gynecologic oncology patients have been published,[3] but uptake has been inconsistent.[4–7] A recent meta-analysis of cohort studies and randomized controlled trials of ERAS in gynecologic oncology reported a mean reduction in length of stay of 1.64 days (95% CI 1.18 to 2.10 days) compared with historical data.[8]

Evidence has mostly been derived from observational studies with heterogeneous ERAS protocols,[9–12] and only a few studies have specifically assessed the effect of ERAS programs in patients undergoing surgery for advanced ovarian cancer.[13] Also randomized studies have to a large degree studied heterogeneous populations of patients with gynecological

cancer.[14 15] However, ovarian cancer patients are in many ways distinctly different from both other gynecologic oncology patients and other surgical patients. Patients are often diagnosed with advanced disease and present with a high symptom burden including dyspnea, nausea, impairment of gastrointestinal function, and malnutrition. These patients are typically not eligible for minimally invasive techniques, and operative procedures often include multivisceral resections with high post-operative morbidity.[16]

Multidisciplinary discussion will select patients for either upfront debulking surgery or administration of neoadjuvant chemotherapy with the aim to reduce disease burden and improve chances of resectability at interval cytoreduction. Attempts have been made to increase radicality to further improve survival outcomes. The randomized PROFAST trial studied ERAS in ovarian cancer patients undergoing debulking surgery and reported reduced length of stay from 9 to 7 days in the ERAS group, with similar rates of complications in the ERAS and control groups (16% and 18%, respectively).[17]

Evaluation of ERAS pathways has primarily focused on traditional measures of healthcare such as length of stay and complication rates. Adherence is seldomly reported and may be crucial to study the full benefit of the program. This study prospectively evaluated the implementation of ERAS in patients undergoing surgery for suspected and advanced ovarian cancer at a large tertiary hospital.

## METHODS

### Study Design and Population

This is a prospective observational cohort study including patients undergoing laparotomy for advanced or suspected ovarian cancer at the department of gynecologic oncology at the Norwegian Radium Hospital, Oslo University Hospital. Patients were prospectively included prior to the implementation of ERAS (pre-ERAS) from May 15, 2017 to May 6, 2018, and after the implementation (post-ERAS) from May 7, 2018 to June 3, 2019. A priori, patients were stratified according to the planned extent of surgery: cohort 1 included patients planned for surgery of advanced (in the majority histologically verified) disease; in cohort 2, patients underwent surgery for a suspicious pelvic tumor. Table 1 includes the key aspects of the ERAS protocol compared with standard of care pre-ERAS.

### Outcome Measures

Clinical data were prospectively collected and validated against the medical records. The age adjusted Charlson Comorbidity Index[18] was used to categorize comorbidity. We used the surgical complexity score developed by Aletti et al to categorize surgical procedures.[19] Surgeries were then categorized into low (score <4), intermediate (score 4–7) and high complexity (score ≥8). Complications were recorded in the department-specific complication registry according to the contracted Accordion classification.[20] Length of stay was calculated from the day of admission until the day of discharge home or the referring hospital. Length of stay was calculated separately for patients residing in the Oslo community, for whom our department serves as the local hospital. The mean daily doses of opioid analgesics were calculated in oral morphine equivalents.

### Statistical Analysis

Descriptive statistics for categorical variables were reported as frequency (%) to describe the demographic and clinical characteristics of patients included. Continuous variables were reported as median and interquartile range (IQR) or mean and standard deviation (SD) where appropriate. The data were analyzed by descriptive and correlation analysis. Group comparisons (ie, before and after implementation of ERAS) were performed using Fisher's exact test for categorical variables and Mann-Whitney U test for continuous variables. All statistical tests were two-sided and done with Stata/SE 16.1 (Stata Corp LP, TX). We considered p values <0.05 to be statistically significant. The Reporting on ERAS Compliance, Outcomes, and Elements Research (RECOvER) checklist for reporting was used.[21]

## RESULTS

### Patient Characteristics

We included 439 women, of whom 243 were in the pre-implementation group and 196 had surgery post-ERAS (Table 1). In the whole cohort, 235 (54%) underwent surgery for advanced ovarian cancer in cohort 1 and 204 (46%) in cohort 2. Baseline characteristics and details on surgical procedures performed are presented in Table 2. Apart from the distribution of the American Society of Anesthesiology (ASA) score, baseline characteristics were similar between the pre- and post-ERAS cohort. There was no difference in the distribution of the two surgical cohorts or surgical complexity between the pre- and post-ERAS group. In the 'advanced' cohort (n=235), 138 (59%) patients were undergoing primary surgery, and 72 (30%) interval debulking surgery. Also in this advanced cohort, there was no difference in surgical complexity pre- and post-ERAS. The remaining patients were categorized as palliative or secondary debulking surgeries. Seventeen percent of the surgeries in cohort 1 were of high surgical complexity and 27% of the patients had at least one bowel anastomosis. Surgical details in cohort 1 are given in Table 3. Key outcome and adherence results in the pre- and post-ERAS cohort are summarized in Table 4.

### Adherence to the ERAS Pathway

Opioid-Sparing Analgesia

After implementation of ERAS, pre-medication with non-steroidal anti-inflammatory drugs (NSAIDs) were given to 46% of the patients versus 0% of the pre-ERAS patients (p≤0.001). Also post-operatively, more patients received NSAIDs with 82% versus 1% receiving at least one dose of parecoxib (p<0.001), and 87% versus 72% receiving at least one dose of celecoxib (p=0.005). In cohort 2 the epidural catheter was removed significantly earlier after the implementation of ERAS (p=0.044) compared with pre-ERAS. At day 3, 76% of the patients had the epidural removed compared with 58% pre-ERAS. There was a significant reduction in oral morphine equivalents to a median of 116 mg in the post-ERAS cohort compared with 136 mg pre-ERAS (p=0.002).

Pre-operative Preparation

Pre-operative fasting times were significantly reduced post-ERAS, both for fluids (median 3.7 hours vs 11.0 hours, p<0.001) and solids (median 13.1 hours vs 16.0 hours, p<0.001). A higher proportion of patients did not receive any

**Table 1** Key elements of ERAS implemented at the department of gynecological oncology, Oslo University Hospital

| Phase | Measures pre-ERAS | Measures post-ERAS |
|---|---|---|
| Pre-operative | ► Oral, not-standardized information, education and counseling | ► Information, education and counseling, preferably together with relatives based on an ERAS-specific leaflet (oral and written)<br>► Stop smoking<br>► Nutritional screening with subsequent nutritional support<br>► Patient diary and information about discharge home criteria |
| Day before surgery (–1) | ► No standardized procedure for bowel preparation for patients in cohort 1, rectal enema for patients in cohort 2<br>► No fluids or solids after 24:00 | ► Standardized procedures for bowel preparation (no routine oral bowel preparation, rectal enema for patients in cohort 1)<br>► No long-acting sedatives<br>► Solid foods until 24:00, encourage light meal 21:00–24:00 |
| Peri-operatively | ► Active body heating<br>► No guidance for nasogastric tubes or drains<br>► Standardized combined anesthetic (including thoracal epidural)<br>► No guidance for fluid management<br>► No specific guidance for vasopressor use | ► Active body heating, specified target temperature ≥36°C<br>► Avoidance of nasogastric tube after surgery<br>► Avoidance of abdominal drains<br>► Standardized combined anesthetic (including thoracal epidural)<br>► Standardized fluid management: maintenance peri-operatively: Ringer's acetate 5 mL/kg/hour, infusion pump is used; antibiotic liquid is included in the fluid balance; extra fluid guided by BT, pulse, urine output, peripheral capillary response, PPV; consider use of Lidco, target MAP >60 mm Hg; consider albumin if colloids are needed; blood loss is replaced with erythrocyte concentrates; FFP if bleeding >50% of the blood volume if bleeding is still ongoing bleeding; fluid balance at the end of the operation; ascites is included in the fluid balance, but not replaced; perspiration and 3-room losses are not included<br>► Liberal use of vasopressor medications |
| Day 0 | ► No guidance for fluid management<br>► No guidance on oral intake | ► 300 mL cordial drink 2 hours before surgery<br>► Standardized fluid treatment: preferably oral intake, target 30 mL/kg/24 hours<br>► Offer a light meal as soon as possible and start with a nutritional drink (Nutridrink Compact Protein 30 mL x 4) |
| Post-operative | ► Encourage early oral intake<br>► Encourage mobilization<br>► No guidance on tapering of epidural<br>► Post-operative management included oral opioids (oxycontin/oxynorm and celecoxib) | ► Standard mobilization including physiotherapy for patients in cohort 1 on day 1 and 2<br>► Continuation of nutritional drink 30 mL x 4<br>► Standardized anti-emetic treatment<br>– 1. choice: droperidol (Dridol)<br>– 2. choice: cyclizine (Valoid/Marzine)<br>– 3. choice: ondansetron (Zofran)<br>– 4. choice: aprepitant (Emend)<br>► Standard postoperative pain treatment (oxycontin/oxynorm and celecoxib), including tapering of epidural<br>► Removal of urinary catheter when epidural <5 mL/h<br>► Prophylaxis for post-operative ileus<br>– Paraffin 30 mL<br>– Chewing gum x 4 for 30 min<br>► Discharge criteria |

BP, Blood pressure; ERAS, enhanced recovery after surgery; FFP, fresh frozen plasma; MAP, mean arterial pressure; PPV, pulse pressure variation.

bowel preparation (32% vs 2%, p<0.001). Still, 34% of the patients in cohort 2 received an enema post-ERAS, although not in line with the ERAS protocol. In cohort 1, 61% had an enema versus 51% pre-ERAS, and 16% had oral bowel preparation versus 47% pre-ERAS. In 17%, no bowel preparation was performed versus 2% pre-ERAS. In the remaining patients, that information was missing. A larger proportion of patients received post-operative nausea and vomiting prophylaxis with ondansetron and dexamethasone (80% vs 64%, p=0.009). A significantly larger proportion of patients had a temperature of ≥36°C at the start of the operation (56% vs 34%, p<0.001). Noteworthy, almost half of the patients were despite the implementation of ERAS not normothermic at the start of surgery.

**Table 2** Baseline characteristics in the study cohort by treatment period (pre-ERAS and post-ERAS)

| Baseline characteristics | | Pre-ERAS (n=243) | Post-ERAS (n=196) | P value |
|---|---|---|---|---|
| Age, median (IQR‡), years | | 63.5 (52.9-71.3) | 64.7 (54.5-72.3) | 0.25 |
| Weight, median (IQR‡), years | | 68.0 (60.8-78.0) | 74.0 (64.0-82.0) | 0.006 |
| Cohort 1, 'advanced' (n=235) | | 118 (49%) | 117 (60%) | 0.021 |
| Cohort 2, 'suspicious pelvic tumor' (n=204) | | 125 (51%) | 79 (40%) | |
| ASA score* (n=435) | I | 23 (10%) | 6 (3%) | 0.041 |
| | II | 166 (69%) | 146 (75%) | |
| | II | 49 (20%) | 38 (20%) | |
| | IV | 3 (1%) | 4 (2%) | |
| Age adjusted Charlson Comorbidity Index (n=439) | <6 | 229 (94%) | 187 (95%) | 0.97 |
| | ≥6 | 14 (6%) | 9 (5%) | |
| Surgical complexity score† (n=439) | Low | 138 (57%) | 113 (58%) | 0.88 |
| | Intermediate | 84 (34%) | 64 (32%) | |
| | High | 21 (9%) | 19 (10%) | |
| Pre-operative anemia, g/dL (n=439) | <12 | 69 (28%) | 59 (30%) | 0.75 |
| Pre-operative albumin, g/L (n=434) | <35 | 20 (8%) | 10 (5%) | 0.25 |
| | ≥35 | 219 (90%) | 185 (94%) | |

*ASA score: American Society of Anesthesiologists physical status classification system.
†Aletti surgical complexity score.[19]
‡IQR: Interquartile range
ERAS, enhanced recovery after surgery.

### Peri-operative Management

Use of epidural was the mainstay of analgesia both pre- and post-ERAS (97% vs 98%). Peri-operative fluid administration was significantly reduced with a median of 11.5 mL/kg/hour (IQR 9.0–15.4) post-ERAS versus 15.8 mL/kg/hour (IQR 10.8–22.5) pre-ERAS (p≤0.001). This reduction was evident in both surgical cohorts. There was also less variation in the volume given during surgery. At the same time, there was an increase in the continuous infusion of vasopressor medication (post-ERAS 77% vs pre-ERAS 58%, p<0.001).

Fewer patients received an intra-abdominal drain after surgery (17% post-ERAS vs 27% pre-ERAS, p=0.013). In the advanced cohort (cohort 1), fewer patients had a nasogastric tube still in place at the end of surgery (3% post-ERAS vs 11% pre-ERAS, p=0.041).

**Table 3** Surgical details in cohort 1 'advanced' pre- and post-ERAS

| | | Pre-ERAS | Post-ERAS | P value |
|---|---|---|---|---|
| Indication | Upfront debulking surgery | 73 (62%) | 65 (56%) | 0.42 |
| | Interval debulking surgery | 31 (26%) | 41 (34%) | |
| | Relapsed disease | 13 (11%) | 11 (9%) | |
| | Palliative surgery | 1 (1%) | 0 | |
| Surgical complexity score* | Low | 47 (40%) | 55 (47%) | 0.54 |
| | Intermediate | 50 (42%) | 43 (37%) | |
| | High | 21 (18%) | 19 (16%) | |
| Peritoneal carcinomatosis index, median (IQR)† | | 15.0 (4.8–22.0) | 14.0 (4.0–26.0) | 0.97 |
| Presence of ascites | | 72 (61%) | 69 (59%) | 0.69 |
| Bowel anastomosis | | 37 (31%) | 27 (23%) | 0.19 |
| Stoma | | 4 (3%) | 6 (5%) | 0.54 |

*Aletti surgical complexity score.[19]
†IQR:Interquartile range
ERAS, enhanced recovery after surgery.

**Table 4** Key compliance and outcome results in the pre- and post-ERAS cohort

| Outcome | | Pre-ERAS | Post ERAS | P value |
|---|---|---|---|---|
| Pre-operative fasting time, median (IQR), hours | Solids | 16.0 (13.0-20.8) | 13.1 (11.7-15.9) | <0.001 |
| | Fluids | 11.0 (9.6-13.5) | 3.7 (3.4-4.7) | <0.001 |
| Multimodal PONV prophylaxis (%) | | 64 | 80 | 0.009 |
| Normothermia (%) | | 34 | 56 | <0.001 |
| Use of EDA (%) | | 97 | 98 | 0.74 |
| Use of abdominal drain (%) | | 27 | 17 | 0.013 |
| Gastric tube at the end of surgery (%) | | 6 | 4 | 0.37 |
| Peri-operative fluid administration, median (IQR), mL/kg/hour | | 15.8 (10.8-22.5) | 11.5 (9.0-15.4) | <0.001 |
| OMEQ, median (IQR), mg | | 136 (97-192) | 116 (80-160) | 0.002 |
| Offered food day 1 (%) | | 54 | 68 | 0.007 |
| Mobilized in room day 0 (%) | | 6 | 20 | <0.001 |
| Thromboembolic prophylaxis (%) | | 100 | 100 | NA |
| LOS in days, mean±SD, days | | 5.5±2.7 | 5.6±2.9 | 0.75 |
| At least one grade 3 complication (%) | | 6 | 16 | 0.023 |
| Readmission rate (%) | | 6 | 5 | 0.68 |

EDA, epidural anethesia; ERAS, enhanced recovery after surgery; IQR, Interquartile range; LOS, length of stay; OMEQ, oral morphine equivalents; PONV, post-operative nausea and vomiting.

### Post-operative Management and Length of Stay

In both surgical cohorts, a significantly larger proportion was offered food on day 0 (68% vs 54%, p=0.007) and was mobilized early (20% on day 0 vs 6%, p<0.001). In cohort 1, 55% were offered food on day 0 post-ERAS compared with 36% pre-ERAS (p=0.011), and 15% were mobilized in their own room on day 0 post-ERAS compared with 0% pre-ERAS (p=0.023). In the whole group, there was no difference in length of stay (mean±SD 5.6±2.9 days post-ERAS vs mean 5.5±2.7 days pre-ERAS). However, in cohort 2 there was a statistically significant reduction in length of stay (mean 4.3±1.5 days post-ERAS vs mean 4.6±1.2 pre-ERAS, p=0.026). In both cohorts together, a larger proportion of patients was discharged directly home as opposed to being transferred to their local hospital (79% post-ERAS vs 51% pre-ERAS, p<0.001). Mean length of stay of patients residing in the Oslo community was separately analyzed, with 5.9±3.4 days post-ERAS versus 6.8±4.6 days pre-ERAS (p=0.32). For the advanced cohort (cohort 1), mean length of stay was 7.1±3.7 days post-ERAS versus 8.8±5.6 days pre-ERAS (p=0.27). For cohort 2, mean length of stay was 4.5±2.43 days post-ERAS versus 4.6±0.88 days pre-ERAS (p=0.19).

### Complications and Readmissions

There were significantly more patients with at least one grade 3 complication post-ERAS (16% vs 6% pre-ERAS, p=0.023). In cohort 1, 23% and 8% had at least one grade 3 complication post-ERAS and pre-ERAS, respectively (p=0.002). In cohort 2, 6% had at least one grade 3 complication both post-ERAS and pre-ERAS (p=1.0). Grade 3 complications in cohort 1 were analyzed in more detail. There was no statistically significant difference in any specific subcategory of complications with the following prevalence of gastrointestinal (post-ERAS 7%, n=8 vs pre-ERAS 3%, n=3), respiratory (post-ERAS 11%, n=13 vs pre-ERAS 4%, n=5), infectious (post-ERAS 2%, n=2 vs pre-ERAS 0%), and other complications (post-ERAS n=4, 3% vs pre-ERAS 0%). A detailed overview of the complications of at least grade 2 in cohort 1 is given in Table 5. There was no statistically significant change in readmissions in the cohort as a whole (5% post-ERAS vs 6% pre-ERAS, p=0.68) or in the pre-defined surgical cohorts (6% post-ERAS vs 8% pre-ERAS in cohort 1, p=0.80; 4% post-ERAS vs 5% pre-ERAS in cohort 2, p=1.0).

## DISCUSSION

### Summary of Main Results

In patients undergoing surgery for suspected or advanced ovarian cancer, implementation of ERAS is feasible, with a high rate of adherence to most ERAS elements. In this large prospective study, length of stay was only reduced for patients undergoing surgery for a suspicious pelvic tumor, without any increase in readmission rate in any of the surgical cohorts. The increase in grade 3 complications necessitates close monitoring and auditing of complications, especially in patients with advanced disease, with careful evaluation of surgical techniques and peri-operative management.

### Results in the Context of Published Literature

This is the largest prospective study of the implementation of an ERAS protocol in separate cohorts of patients undergoing surgery for suspected or advanced ovarian cancer. It differs therefore in design from most published cohort studies, where outcome data often are compared with retrospective historical data or where only a minority of patients were undergoing surgery for ovarian cancer.[13] Results have only been seldomly reported separately for patients with advanced disease. There are a few randomized controlled

**Table 5** Overview of the complications of at least grade 2 in cohort 1 according to contracted Accordion classification

| | Grade | Pre-ERAS | Post-ERAS | P value |
|---|---|---|---|---|
| Gastrointestinal complications | ≥2 | 8 (3%) | 11 (6%) | 0.25 |
| Genitourinary complications | ≥2 | 0 | 3 (2%) | 0.088 |
| Urinary tract infection | ≥2 | 19 (8%) | 16 (8%) | 1.0 |
| Infection* | ≥2 | 28 (12%) | 26 (13%) | 0.86 |
| Skin/wound complications | ≥2 | 18 (7%) | 10 (5%) | 0.43 |
| Anemia | ≥2 | 46 (19%) | 37 (19%) | 1.0 |
| Cardiovascular complications | ≥2 | 6 (2%) | 8 (4%) | 0.41 |
| Respiratory complications | ≥2 | 7 (3%) | 15 (8%) | 0.028 |
| Neurological complications | ≥2 | 0 | 1 (1%) | 0.31 |
| Metabolic complications | ≥2 | 2 (1%) | 1 (1%) | 1.0 |
| Other | ≥2 | 20 (8%) | 18 (9%) | 0.74 |

*Including urinary tract infection, excluding skin/wound infections.
ERAS, enhanced recovery after surgery.

trials evaluating ERAS in gynecologic oncology, either full ERAS protocols[14 15] or single interventions,[22 23] but only one enrolled specifically patients with ovarian cancer.[17]

Our ERAS protocol also covers all aspects of a contemporary ERAS protocol as outlined in recent guidelines.[3] Compliance with a higher number of ERAS items has been associated with fewer complications and shorter length of stay,[24 25] but has only rarely been reported in published cohort studies. In the PROFAST trial, an overall compliance of 92% was reported without providing details on how compliance was measured.[17] The introduction of an ERAS protocol at our institution led to significant changes in clinical management and a higher adherence rate to international guidelines such as guidelines on fasting,[26] fluid management, use of vasopressor medications, and post-operative nausea and vomiting prophylaxis.[27] Although peri-operative fluid administration depends on a variety of hemodynamic variables, fluid overload can be prevented by balancing fluids and vasopressor medications.[28] Implementation of structured care pathways such as ERAS will therefore improve clinical care by increasing the adherence to best evidence care, and monitoring of the results will generate baseline data for continuous quality improvement programs.

The majority of studies of ERAS, also in gynecologic oncology, have focused on length of stay as outcome measure. The most significant shortenings of 1–2 days have been reported in mixed gynecologic oncology cohorts undergoing less extensive surgery[29] or in patients undergoing complex surgery with longer length of stay prior to the implementation of ERAS (eg, 9–13 days on average).[17 30 31] In our study, even pre-ERAS, mean length of stay for patients with advanced disease (cohort 1) was only 8.8 days for patients residing in the Oslo community who were not transferred to another local hospital after initial recovery. Although length of stay was numerically shorter in the ERAS group (7.1 days), the difference was not statistically significant. A significant reduction in length of stay in cohort 2 was observed for the cohort as a whole, but not specifically for patients residing in Oslo.

This reduction in length of stay may be due to higher awareness and strict application of discharge criteria, the earlier removal of epidural anesthesia and urinary catheter as well as improved patient preparedness for discharge when managed within an ERAS pathway. Also reports on reduced readmission rates need to be interpreted in the context of pre-ERAS data. The PROFAST study reported decreased readmission rates in the ERAS group but had very high readmission rates in the control group (20%). Our readmission rates of 6% and 8%, post- and pre- ERAS, respectively, are comparable or lower than what was reported in a recent review of patients undergoing cytoreductive surgery for ovarian cancer.[32] This might explain why we did not observe a significant reduction in readmission rates after implementation of ERAS.

The heterogeneity in reporting of complications in studies evaluating ERAS protocols makes a direct comparison difficult, but major complications are still common in patients undergoing surgery for advanced ovarian cancer. Major complications have been reported in 17–21% and up to 35% in patients with high surgical complexity,[33–35] independent of ERAS. The PROFAST trial did not report any significant difference in complication rates, with 16% and 18% of patients experiencing major complications in the ERAS and control group, respectively. The reported prevalence of major complications in our study is in line with these reports. We could not identify a single category of complication driving the increase in grade 3 complications post-ERAS and are uncertain about the causal relationship between ERAS implementation and the increase in major complications. The difference in baseline weight, with higher weight in patients treated in the ERAS cohort, may have contributed to the higher rate of complications. Still, the awareness and careful review of serious complications have led to a quality improvement program of our surgical service. Focus on adherence to the bowel preparation protocol in ERAS as well as modification of the surgical technique with sparing of the superior rectal artery in patients with anterior colonic resection were direct consequences of the monitoring of the ERAS implementation. Consequent auditing in a multidisciplinary team, identification of barriers and re-implementation is therefore crucial to fully exploit the potential of ERAS. A structured prehabilitation program may provide the optimal framework for further optimization prior to surgery,[36] with the aim of reducing complication rates.

## Strengths and Weaknesses

The strength of our study is the prospective collection of data post- and pre-ERAS and the detailed assessment of compliance to ERAS elements. We report data specifically on patients undergoing surgery for advanced disease, presenting the largest prospective series reported to date on such patients. This is not a randomized controlled trial, and even if there were no significant differences in baseline characteristics including surgical complexity score and weight, we cannot rule out that differences in patient population post- and pre-ERAS may have biased our results. Clinical care in our institution is guideline-based and does to a much lesser degree depend on the attending gyne-oncologist/anesthetist. Even though the project group had started the process of drafting the new guidelines, these were not implemented before data collection in the post-ERAS cohort. Thus, there was very little dilution of practice before the implementation of ERAS.

## Implications for Practice and Future Research

This large prospective cohort study confirms the feasibility of an ERAS protocol for patients with suspected ovarian cancer as well as for patients with advanced disease. A structured care pathway increases adherence to evidence-based guidelines of peri-operative management and harmonization of practice. The prevalence of serious complications in patients undergoing debulking surgery calls for continuous performance audits, quality improvement work, and further research on optimization of ERAS and prehabilitation programs.

**Author affiliations**
[1]Department of Gynecological Oncology, Oslo University Hospital, Oslo, Norway
[2]Faculty of Medicine, Institute for Clinical Medicine, University of Oslo, Oslo, Norway
[3]Institute for Cancer Genetics and Informatics, Oslo University Hospital, Oslo, Norway
[4]Department of Informatics, University of Oslo, Oslo, Norway
[5]Department of Clinical Service, Oslo University Hospital, Oslo, Norway
[6]Department of Gastroenterological Surgery, Oslo University Hospital, Oslo, Norway
[7]Department of Anesthesia and Intensive Care Medicine, Division of Emergencies and Critical Care, Oslo, Norway

**Acknowledgements** We would like to thank Prof. Dr. Dr. h.c. Andreas du Bois, Dr. Philipp Harter and Dr. Stephanie Schneider at the Department of Gynecology and Gynecological Oncology, Kliniken Essen Mitte, Essen, Germany for their collaboration in setting up the data collection sheet and for the scientific discussions around ERAS when we planned this project. We also thank all staff members at our department for their contribution to data collection and commitment to ERAS. We further acknowledge the support of Farah Naseem and cand med Tuan-Khanh Nguyen in data collection. We would like to thank the MUHC Patient Education Office, McGill University Health Center, Quebec, Canada for their support throughout the development of the patient education material.

**Contributors** KL: Project initiation, design and methodology, project oversight including funding acquisition. Monitoring of data collection, ethical appproval. Drafted the initial version of the manuscript, revision of the paper. AK: Statistical analysis plan and statistical analysis. Interpretation of results. Contributed to initial draft of the manuscript. Full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. BE: Project design, data collection, interpretation of results, revising the manuscript. SHD: Data collection, interpretation of results. YYW: Design data collection tools, data collection. AG-HH/SLW: Project design, design data collection tools, interpretation of results. OM/GAN/SH: Project design, interpretation of results. KEJ-H: Project design, interpretation of results. UK: Design and methodology, interpretation of results, contributed to initial draft of the manuscript. All authors contributed to revision of the final manuscript. They read and approved the final version of the paper.

**Funding** This work was supported by the Radiumhospitalets Legater.

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants. Approval from the Oslo University Hospital integrated data protection authority was granted on July 4, 2017 (id: 2017/7007). Patient privacy was protected by coding and processing all data anonymously. A waiver for patient consent was granted.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. We will provide our data for the reproducibility of this study in other centers if such is requested. Such sharing would require approval by the data protection office at Oslo University Hospital.



**ORCID iDs**
Kristina Lindemann http://orcid.org/0000-0002-2162-0175
Andreas Kleppe http://orcid.org/0000-0002-8370-5289

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