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Quality of life after early enteral feeding versus standard care for proven or suspected advanced epithelial ovarian cancer: Results from a randomised trial ☆

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HIGHLIGHTS

- Enteral feeding has been proposed as the preferred way to deliver caloric intake.
- Early enteral feeding may improve nutritional status in patients with EOC.
- Did not significantly improve patients' QoL or LOS compared to standard of care

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ABSTRACT

Background. Malnutrition is common in patients with advanced epithelial ovarian cancer (EOC), and is associated with impaired quality of life (QoL), longer hospital stay and higher risk of treatment-related adverse events. This phase III multi-centre randomised clinical trial tested early enteral feeding versus standard care on postoperative QoL.

Methods. From 2009 to 2013, 109 patients requiring surgery for suspected advanced EOC, moderately to severely malnourished were enrolled at five sites across Queensland and randomised to intervention (n = 53) or control (n = 56) groups. Intervention involved intraoperative nasojejunal tube placement and enteral feeding until adequate oral intake could be maintained. Despite being randomised to intervention, 20 patients did not receive feeds (13 did not receive the feeding tube; 7 had it removed early). Control involved postoperative diet as tolerated. QoL was measured at baseline, 6 weeks postoperatively and 30 days after the third cycle of chemotherapy. The primary outcome measure was the difference in QoL between the intervention and the control group. Secondary endpoints included treatment-related adverse event occurrence, length of stay, postoperative services use, and nutritional status.

Results. Baseline characteristics were comparable between treatment groups. No significant difference in QoL was found between the groups at any time point. There was a trend towards better nutritional status in patients who received the intervention but the differences did not reach statistical significance except for the intention-to-treat analysis at 7 days postoperatively (11.8 intervention vs. 13.8 control, p 0.04).

Conclusion. Early enteral feeding did not significantly improve patients' QoL compared to standard of care but may improve nutritional status.

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1. Introduction

Epithelial ovarian cancer (EOC) represents approximately 90% of all malignant ovarian tumours and is associated with a worse prognosis compared to other gynaecologic malignancies [1]. World-wide, an estimated 238,719 women were diagnosed with, and 151,917 died from ovarian cancer in 2012 [2,3]. Similar to the United States, ovarian cancer has the sixth highest mortality rate of all cancers in women in Australia after cancers of the lung, breast, colon, pancreas and unknown primary site, and supportive care treatments to improve survival are urgently needed [4,5].

The location of ovarian tumours deep within the pelvis and abdomen, along with usually nonspecific symptoms and ineffective screening makes early diagnosis difficult, thus patients tend to present late with advanced stages of EOC (III and IV) [1,6]. Treatment typically involves a combination of extensive cytoreductive surgery and intensive chemotherapy for several months [1]. The treatment results in considerable physical, psychological, social and economic impacts [1].

Abdominal bloating, tumour load, ascites, pleural effusions and even subclinical bowel obstruction are associated with the presence of advanced EOC and reduce the patient's ability to eat, leading to worsening nutritional status [1,6]. Ovarian cancer patients have a 19-times higher odds to be malnourished at diagnosis compared with patients with benign gynaecological disease [7]. Malnutrition is also associated with impaired quality of life (QoL) and longer hospital stay, as well as higher risk of treatment-related adverse events following surgery [6,8].

Among patients with various types of gynaecological cancer, several studies have shown early oral diet to be associated with reduced length of hospital stay, reduced postoperative discomfort and faster resolution of postoperative ileus following surgery [6]. However, many patients may not achieve an adequate intake for the first few days after surgery, and for a patient who enters surgery in a malnourished state this may increase their likelihood of worse treatment outcomes and reduced QoL. In patients treated for other cancers where malnutrition is an issue, enteral feeding has been tested and found to be beneficial [9–15].

These studies have been performed mainly in patients with gastrointestinal and lung malignancies, as well as in patients undergoing radiotherapy for head and neck cancers [9–15]. They consistently reported improved outcomes of the nutritional interventions including a reduction in postoperative complications [9,10,16], a shorter length of hospital stay [9,10,13], an improvement in protein metabolism [13], or reduction in weight loss [15] and some concluded that it is cost-effective to support patients with enteral feeding [12,13,17]. Compared to standard care, which means oral diet as tolerated, studies have found a nutritional benefit of enteral feeding in adult patients with colorectal and gastric cancer, and paediatric patients with brain tumours, myeloid leukaemia or high-risk solid tumours [18–20]. These patients receiving enteral feeding were found to have significantly better nutritional status and immune function, and accelerated recovery following surgery [18,19].

Enteral feeding may improve epithelial structure and function [21,22], enhance mucosal immunity [23], and reduce the risk of bacterial translocation. In patients with functioning gastrointestinal tracts, enteral feeding is preferred for nutritional support over the parenteral route due to lower risk of infections, lower costs, and shorter length of stay in hospital [9,10,24].

However, there is a lack of studies examining the effects of enteral feeding after surgery on outcomes specifically for EOC patients. Enteral feeding has been proposed as the preferred way to deliver caloric intake, because it is less invasive than total parenteral nutrition and its complication rates are lower [9,10].

We report findings from a prospective, randomised, multi-centre clinical trial investigating whether early postoperative enteral nutrition for malnourished women with advanced EOC can improve their QoL, nutritional status, perioperative and postoperative outcomes compared to control.

2. Methods

2.1. Ethical approval

All relevant hospital and university human research ethics committees approved this trial. The OPEN trial is registered with ClinicalTrials.gov, number NCT00850772.

2.2. Participants

Participants were enrolled through one of five participating sites in Queensland, Australia, and were eligible for inclusion if they required planned upfront or interval cytoreductive surgery for suspected or proven advanced EOC, primary peritoneal cancer or fallopian tube cancer; had signs of moderate or severe malnutrition defined as Patient-Generated Subjective Global Assessment (PG-SGA) category B or C; were medically fit for cytoreductive surgery; signed a written informed consent; and were females aged 18 years or older. Participants were excluded if they had other cancers, or recurrent EOC; if they had contraindications to enteral feeding such as ileus, gastrointestinal ischaemia, bilious or persistent vomiting, or mechanical obstruction; if they had a positive urine pregnancy test; or if they were unfit for surgery, at the discretion of the investigator.

2.3. Randomisation and masking

Randomisation was performed centrally, after stratification by treatment site and mode (upfront surgery vs. neoadjuvant chemotherapy). Masking was not possible due to the nature of the treatment; sham treatment was not used due to ethical concerns.

2.4. Procedures

All patients completed a PG-SGA questionnaire to assess their nutritional status. Patients meeting the inclusion criteria for the study were asked for written informed consent to participate in the study.

Enrolled participants were asked to complete the baseline QoL assessment and a demographic questionnaire. All participants underwent medical imaging of the pelvis, abdomen and chest for staging, had a serum biochemistry including serum albumin, full blood count, serum tumour markers (CA 125, CA 19.9, CEA) taken and also received a 12-lead electrocardiogram as per routine preoperative work-up. At baseline, participants received a physical examination, weight and height measurements.

The intervention group underwent insertion of a soft, fine-bore nasojejunal tube inserted by the anaesthetist during surgery, through the participant's nostrils and forwarded into the proximal small bowel. The tubes were fitted with a guide wire and a weighted tip. The location of the nasojejunal tubes was checked by the surgeon via manual palpation intraoperatively and was confirmed by plain X-ray postoperatively prior to the commencement of feeding. Iso-osmolar feeds, continuous over 24 h were used for postoperative feeding. A standard fibre-containing, high-protein enteral nutrition formula (4.2 kJ/mL or 1 kcal/mL) was fed through the nasojejunal tube postoperatively. This standard feed contains 20% protein, 30% fat and 50% carbohydrate. Feeding was commenced at a rate of 40 ml/h at 4 h for the first 24 h. Then, feed rates were increased to provide participants nutrition of 125 kJ/kg body weight, adjusted using standard methodology for overweight patients. Participants randomised to this group were monitored daily by a nutritionist and had their diet modified according to these assessments. Enteral feeding was ceased once the participant was able to maintain an adequate oral intake, defined as 65–75% of the daily nutritional requirements.