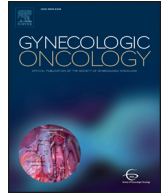




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## Gynecologic Oncology

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## Nutrition interventions in patients with gynecological cancers requiring surgery

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### HIGHLIGHTS

- The tested early oral feeding and enteral feeding interventions were safe.
- Some reported reduced LOS, intestinal recovery time or complications.
- Increasing use of neoadjuvant treatment may reduce the prevalence of malnutrition.

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### ABSTRACT

**Objective.** Including developing countries, between 20 and 88% of gynecological oncology patients may present with at least mild malnutrition at diagnosis. Significant morbidity and mortality is attributed to malnutrition. Here we reviewed randomized clinical trials of nutritional interventions used to achieve early return to oral diet, enhance recovery from surgery and reduce adverse events in gynecological cancer patients undergoing surgery.

**Methods.** Ebscohost (CINAHL + Medline + PsycINFO), Cochrane, Embase, PubMed and Scopus databases were searched for articles published from 2000 onwards. Potentially eligible articles were screened by two reviewers. Length of hospital stay (LOS), postoperative complications, recovery of intestinal function, quality of life (QOL), hematological and immunological parameters were outcome measures of the nutritional interventions.

**Results.** Seven randomized clinical trials were included in the review. Early clear liquid diet, semiliquid diet, regular diet or immune-enhanced enteral diets were all found to be safe as nutritional interventions. In five of the seven trials significantly better outcomes were observed in the intervention group compared to usual care for one or more of the outcomes intestinal recovery time, LOS, postoperative complications and immunological parameters. However, the nutritional interventions varied greatly between the trials, making it difficult to directly compare their findings. Trial quality was low to moderate. Recommended malnutrition screening and assessment tools and guidelines for treatment are reviewed.

**Conclusions.** From the limited findings it would appear that nutritional interventions of early oral feeding and enteral feeding are safe. Receiving nutritional interventions seems to reduce LOS, intestinal recovery time and postoperative complications for some patients. Increasing use of neoadjuvant treatment may reduce the prevalence of patients presenting malnourished for surgery in the future.

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### 1. Introduction

Gynecological cancer presents a major public health concern worldwide. In the USA alone an estimated 100,000 new cases of gynecological

(Cervical, Ovarian, Uterine, Vaginal and Vulvar) cancer are diagnosed each year, with approximately 30,000 deaths occurring annually [1]. Symptomatology, availability of screening tests and whether or not patients are commonly diagnosed at early (endometrial cancer) or late stages of disease (ovarian cancer) differ between the gynecological cancer diagnoses subgroups. Regardless of the cancer type however, presentation of late stage gynecological cancers is still common [2–4]. As cancers grow, they produce an increased metabolic demand. If left unchecked, this progressively contributes to a decline in nutritional status,

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often recognized when patients first present for diagnosis. It has been reported that malnutrition may be responsible for 20% of gynecological cancer deaths [5,6].

Malnutrition can be defined as a state of deficiency, excess or imbalance of nutrients, causing adverse effects in bodily functions or form [7]. While malnutrition constitutes of both over and undernutrition, studies in gynecological cancer patients undergoing surgery largely focus on undernutrition. The most relevant features describing undernutrition are deficiency in energy, protein and/or decrease in fat free mass. This negative nutritional balance can eventually lead to reduced physical or mental capacity, and adverse clinical outcomes [8,9]. People affected by other chronic diseases in addition to gynecological cancer, are particularly predisposed to the risk of malnutrition. As many as 40 to 80% of all cancer patients are estimated to experience malnutrition at some stage during the clinical course of their disease [10]. Cancer cachexia in contrast is a complex metabolic syndrome caused by cancer. Cachexia differs from malnutrition, as it is a hyper-catabolic state resulting in accelerated muscle loss adjacent to chronic inflammatory responses in the body. Although weight loss is common in cancer patients who are malnourished, weight loss as a result of cachexia is not caused by an inadequate caloric intake alone. While most malnourished cases can be treated with aggressive feeding to increased caloric intake, weight loss in cachexia is not easily reversed [11].

Contemporary studies conducted in Australia and USA, have shown that between 20 and 53% of gynecological cancer patients present with at least mild malnutrition at diagnosis [12,13] (Table 1). Prevalence of malnutrition has been reported to be even higher in developing nations (62–88%) [14–16] (Table 1). Studies reporting these estimates based on malnutrition screening or assessment tools are summarized in Table 1.

The British Association for Parenteral and Enteral Nutrition (BAPEN) listed a number of social and physical factors which increase the risk of malnutrition, including social isolation, poverty and cultural norms. Painful mouth/teeth, swallowing difficulties, loss of smell/taste or limited mobility are physical factors that can contribute to the increased risk of malnutrition. Other risk factors include, being over the age of 65 years, high use of drugs, alcohol, or cigarettes or having a chronic progressive condition [17]. Given the high prevalence of malnutrition, and the increased risk of adverse events during surgery in malnourished patients, it was the aim of this review to summarize evidence from randomized clinical trials to reduce the risk of malnutrition, enhance recovery after surgery, and achieve early return to oral diet in the

gynecological cancer setting, and relate the evidence to current guidelines for screening, assessing and overcoming malnutrition.

## 2. Methods

### 2.1. Search strategy

We searched Ebscohost (CINAHL + Medline + PsycINFO), Cochrane, Embase, PubMed and Scopus. Articles were restricted to human research, published in English and between 01/01/2000 to 25/11/2016. The search terms used were: “female genital neoplasm; nutritional support; malnutrition; nutrition; quality of life (QOL); length of stay (LOS); treatment outcome; perioperative care; postoperative care; gynecological surgical procedure; nutritional risk assessment; randomized trial”. The search terms were combined and adjusted to suit each database search builder, details can be seen in supplementary Table 1. A total of 443 potential articles were identified. Reviews, meta-analyses, descriptive studies, or those investigating biomarkers were ineligible. After screening title, abstract and full text of these potentially eligible articles a total of seven articles were included in the final review. Fig. 1 shows a visual of the search strategy and flow of studies. Quality criteria of the studies were assessed and summarized in supplementary Table 3.

## 3. Results

### 3.1. Patients and study characteristics

A total of seven randomized controlled trials fulfilled the inclusion criteria (a summary of the studies' main characteristics is provided in Table 2; details are in supplementary Table 3). All seven studies evaluated interventions for improving nutritional recovery in gynecological cancer patients undergoing cancer-related surgery. The study participants were all adult females, 18–85 years of age. The sample size within the studies ranged from 40 to 245 participants. The studies were conducted across a number of countries including Australia, Canada, China, Italy, Turkey and the USA. Six of the seven studies had mixed gynecological cancer samples, while Baker et al. [18] only included patients with ovarian cancer. The majority of studies (n = 5) did not report the stage of cancer. The most common surgical procedures

**Table 1**  
Prevalence of malnutrition in gynecological cancer studies.

Study	Cancer type	Sample size	Age range (years)	Prevalence of malnutrition	Measuring tool
Das et al., 2014	Various gynecological cancers	60	13–74	Class A = 12% Class B = 48% Class C = 40%	PG-SGA
Gupta et al., 2010	Ovarian cancer	98	31–82	Class A = 47% Class B = 29% Class C = 24%	SGA
Hertlein et al., 2014	Gynecological cancers	272	18–97	Score 0 = 27% Score 1–2 = 31% Score > 3 = 42%	NRS-2002
Laky et al., 2007	Various gynecological cancers	145	20–91	Class A = 80% Class B = 20% Class C = 0	PG-SGA
Laky et al., 2008	Various gynecological cancers	194	20–91	Class A = 76/76% Class B = 23/22% Class C = 1/2%	SGA/PG-SGA
Rodrigues et al., 2015	Various gynecological cancers	146	NA	Class A = 38% Class B = 47% Class C = 23%	PSG-SGA
Yim et al., 2016	Ovarian cancer	213	22–81	Non-mild risk = 78% Moderate-severe risk = 22%	NRI

Abbreviations: NRI: Nutritional Risk Index, NRS-2002: Nutritional Risk Screening-2002, PG-SGA: Patient Generated Subjective Global Assessment, SGA: Subjective Global Assessment. Malnutrition Classification: NRS-2002 classifies patients into: Score 0 = low risk of malnutrition, Score 1–2 = medium risk of malnutrition, >3 = high risk of malnutrition. SGA and PG-SGA classify patients into: Class A - well-nourished, Class B - moderately malnourished, Class C - severely malnourished.

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