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# Influence of gum chewing on postoperative bowel activity after complete staging surgery for gynecological malignancies: A randomized controlled trial

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## HIGHLIGHTS

- Gum chewing is associated with faster recovery of bowel function after complete surgical staging for malignant gynecologic disease.
- Gum chewing is safe, practical, inexpensive, and well tolerated.
- Gum chewing should be used in routine practice with postoperative care of gynecologic oncology.

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## ABSTRACT

*Objective.* To investigate whether gum chewing affects the return of bowel function after complete staging surgery for gynecologic malignancies.

*Methods.* A total of 149 patients undergoing abdominal complete surgical staging for various gynecological cancers were randomized into a gum-chewing group (n = 74) or a control group (n = 75). The patients chewed sugarless gum three times from the first postoperative morning until the first passage of flatus. Each chewing session lasted 30 min. Total abdominal hysterectomy with systematic pelvic and para-aortic lymphadenectomy was performed on all patients as part of complete staging surgery. Groups were compared in terms of time to first bowel movement time, first flatus and feces pass time, postoperative analgesic and antiemetic drug requirement, postoperative oral intake tolerance, mild ileus symptoms and hospital stay.

*Results.* The mean time to flatus (34.0 ± 11.5 *vs.* 43.6 ± 14.0 h; $p < 0.001$), mean time to defecation (49.6 ± 18.7 *vs.* 62.5 ± 21.5 h; $p < 0.001$), mean time to bowel movement (41.5 ± 15.7 *vs.* 50.1 ± 15.9 h; $p = 0.001$), mean time to tolerate diet (4.0 ± 0.8 *vs.* 5.0 ± 0.9 days; $p < 0.001$), mean length of hospital stay (5.9 ± 1 *vs.* 7.0 ± 1.4 days; $p < 0.001$) were significantly reduced in patients that chewed gum compared with controls. Mild ileus symptoms were observed in 27 (36%) patients in the control group compared to 11(14.9%) patients in the gum-chewing group [relative risk, 2.4; 95% confidence interval, 1.2–4.5; $p = 0.004$]. Severe symptoms were observed in two patients (2.7%) in the control group.

*Conclusions.* Gum chewing early in the postoperative period following elective total abdominal hysterectomy and systematic retroperitoneal lymphadenectomy hastens time to bowel motility and ability to tolerate feedings. This inexpensive and well-tolerated treatment should be added as an adjunct in postoperative care of gynecologic oncology.



## Introduction

A delay in the return of normal bowel function with the passage of flatus and feces is one of the most important factors affecting early recovery and discharge in patients undergoing open complete staging surgery for gynecological malignancies. A prolonged hospital stay increases the risk of hospital-acquired infections, deep vein thrombosis, pulmonary compromise and total hospital costs [1]. A variety of procedures have been implemented for management bowel function, including adequate pain control [1], epidural anesthesia [2], gum chewing [3–5], laparoscopic surgery [6], drugs such as metoclopramide, erythromycin, neostigmine, alvimopan [1,7,8], and supportive strategies including nasogastric decompression [9], intravenous fluids [10], and early enteral feeding [11,12].

Gum chewing is a simple, inexpensive and harmless intervention for early recovery of bowel function after gastrointestinal surgery [3], radical cystectomy [4], and cesarean section [5]. However, the favorable effects of gum chewing on return of gastrointestinal function in patients

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undergoing elective total abdominal hysterectomy and systematic retroperitoneal lymphadenectomy have not been investigated. The aim of this randomized controlled trial was to assess the effectiveness of gum chewing on postoperative bowel function in patients undergoing abdominal complete staging surgery for gynecological malignancies.

## Materials and methods

This study was conducted from January 21, 2012–April 20, 2013 at Tepecik Education and Research Hospital, Department of Gynecologic Oncology, Izmir, Turkey. Approval for the study was obtained from the hospital ethics committee and it was registered with the federal government (NCT01835119).

Female patients preparing for complete surgical staging for malignant gynecologic disease such as endometrial cancer, cervix cancer and ovarian cancer were assessed for eligibility. Systematic retroperitoneal lymphadenectomy was performed up to the level of the left renal vein in a greater proportion of cases. Exclusion criteria for the study included thyroid diseases, inflammatory bowel disease, complaints of chronic constipation (defined as two or fewer bowel movements per week), a history of prior abdominal bowel surgery, abdominal radiation, or neoadjuvant chemotherapy, need for intensive care more that 24 h postoperatively, nasogastric tube drainage beyond the first postoperative morning, or bowel anastomosis and upper abdominal multivisceral surgical approaches in relation to the debulking surgery.

The study information was explained to all enrolled subjects, informed written consent obtained and randomization performed as soon as the patients were admitted to our gynecologic oncology service. Eligible patients were randomly assigned to one of two groups by an investigator (I.E.E.) by consecutive opening of sequentially numbered, opaque, sealed envelopes. Envelope randomization was performed by a computer-generated code using the blocked randomization method. Group A acted as the control group and received no treatment, and Group B received sugar-free peppermint-flavored chewing gum.

The same evidence-based protocol of perioperative management, except for chewing gum, was used for all patients. On the day before surgery, patients received a clear liquid diet and bowel preparation with 20-g MgO (Magnesi Kalsine Toz®, İstanbul İlaç, Istanbul, Turkey) and 28.5-g $NaH_2P$ + 10.5-g $Na_2HP$ (BT Enema®, Yenisehir Laboratory, Ankara, Turkey), low-molecular-weight heparin, and prophylactic intravenous antibiotics at induction of anesthesia. Three consultant anesthesiologists who used the same anesthetic technique provided general analgesia with or without an epidural anesthetic. Surgery was perormed *via* a sub-supra umbilical vertical midline incision. All patients underwent total abdominal hysterectomy with systematic pelvic and para-aortic lymph node dissection as part of their staging procedures. The same surgical team performed all operations.

All subjects received the same postoperative care regimen, including the prokinetic agent metoclopramide as an antiemetic if required, stress gastritis prophylaxis in the form of histamine $H_2$ blockers, and low-molecular-weight heparin for 48 h after surgery. The nasogastric tube was removed on the first postoperative morning. Following the removal of the epidural catheter, patients were placed on regular oral paracetamol. Additional opioid or nonsteroidal analgesia was provided when required and their use documented carefully. All patients received standard chest physiotherapy and were mobilized as soon as possible in the postoperative period. Other antiemetic agents were prescribed for nausea if required. No opioid antagonists were used postoperatively.

To reduce the effects of other variables, the postoperative feeding regime was standardized for the study patients: 30–60 ml of water and if tolerated other liquids were started from the first postoperative day until the first passage of flatus. Upon passing flatus, clear fluids and if tolerated semiliquid fiberless diet was allowed. Patients were allowed to progress to a solid diet according to the patient's toleration or the passage of feces. Group B began chewing gum on postoperative day one and chewed gum three times daily. Each chewing lasted 30 min. The administration of therapy was implemented by nursing ward staff and recorded in the patients file. All gum-chewing patients completed their course of gum chewing until the return of bowel function.

The nature of the study did not permit complete blinding after assignment of intervention. Criteria for hospital discharge included stable vital signs with no fever for at least 24 h, ability to ambulate without assistance, ability to tolerate solid food without vomiting, normal urination, and absence of other postoperative complications.

The main outcome variable of the study was postoperative first flatus and defecation time (hours from end of operation). Secondary outcome measures included time to first bowel movement (hours from end of operation), time to tolerate diet, antiemetic need, additional analgesic requirement, tolerance of gum chewing in the study group, postoperative ileus (PI) rate, and length of hospital stay. Time to first bowel movement was defined as hearing the first bowel sound during postoperative routine control.

PI was considered resolved after the first passage of flatus and in the absence of abdominal distention or vomiting. Symptoms were classified as mild, if they spontaneously resolved in a few days with observation and basic support, moderate if vomiting was persistent and a nasogastric tube re-insertion was clinically necessary, and severe if symptoms persisted for more than two days, or resisted previous treatment.

An outcome assessor, who was blinded to the study allocation, evaluated the symptoms and signs of ileus three times daily. To be able to precisely monitor the recovery of bowel function, patients were instructed to notify ward nurses or investigators immediately after the first passage of flatus or a bowel movement and defecation. We checked every patient's bowel sounds using a standard stethoscope six times per day beginning 24 h postoperatively until first bowel sounds were noticed. To accurately monitor recovery of bowel function, patients were instructed to notify nurses or study investigators immediately after they passed either gas or they feeled a bowel movement.

At the start of this randomized controlled trial, all of the studies that addressed gum chewing involved patients with colonic surgery, cesarean section, or radical cystectomy. Thus, we conducted a non-blinded pilot trial of 20 patients in each group (A and B) before the full trial. In Group A, the mean time to flatus was 39.7 ± 12.9 h and in Group B it was 33.1 ± 11.6 h. On this basis, power analysis determined that with a power of 80% and an $\alpha$ level of 0.05, a sample size of 66 patients in each group was required. An additional 10 subjects were recruited to account for possible attrition.

Med Calc version 9.3 was used for statistical analyses. Analysis was done on an intention-to-treat basis. Normal distribution of continuous variables was assessed by the Kolmogorov–Smirnov test. The $\chi^2$ test was used for analysis of categorical variables, Student's *t*-test was used for normally distributed variables in the analysis of continuous variables, and the Mann–Whitney *U*-test was used for variables that were not normally distributed. Relative risk (RR) with 95% confidence interval (CI) was calculated. P values $< 0.05$ were considered to indicate statistical significance. Survival curves were created using Kaplan–Meier analysis.

## Results

Of the 203 eligible patients, 152 were enrolled; 77 patients were randomly assigned to the control Group A and 75 to the gum-chewing Group B. Two patients in the control group and one in the gum group did not enter the study following randomization because they no longer fulfilled the inclusion criteria. In total, 75 patients in the control group and 74 in the gum group were analyzed. The reasons for pre- and post-randomization exclusions are shown in Fig. 1. Baseline demographic data and clinical characteristics of the two study groups were similar and are presented in Table 1.

Patients in both groups had similar operative characteristics, including mean duration of surgery, type of hysterectomy, mean number of removed pelvic and para-aortic lymph nodes, rate of appendectomy,

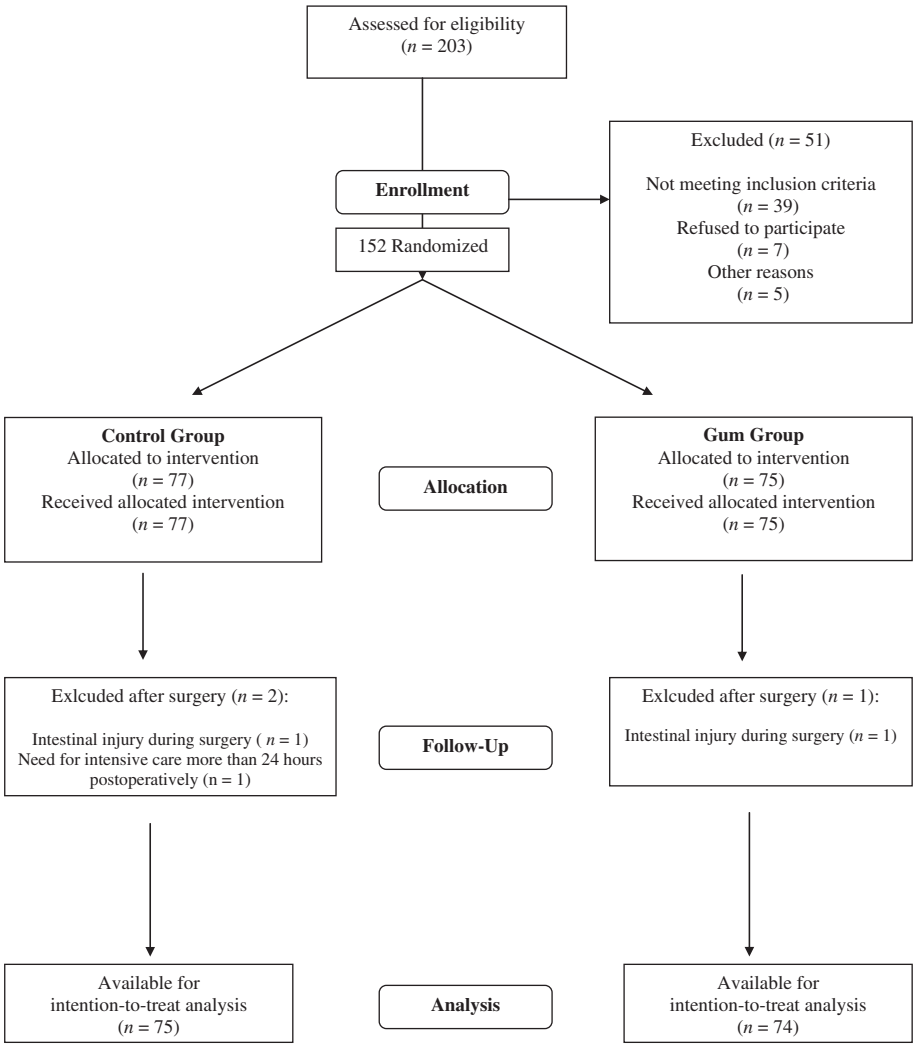


**Fig. 1.** Flow diagram of trial recruitment and follow-up.

douglas peritonectomy, and extensive adhesiolysis (Table 2). All gum-chewing patients tolerated and completed their course of gum chewing until bowel function. There were no reports of any adverse events in relation to gum chewing during the study.

Postoperative clinical outcomes are demonstrated in Table 3 and Fig. 2. The mean time to flatus (34.0 ± 11.5 *vs.* 43.6 ± 14.0 h; $p < 0.001$), mean time to defecation (49.6 ± 18.7 *vs.* 62.5 ± 21.5 h; $p < 0.001$), mean time to bowel movement (41.5 ± 15.7 *vs.* 50.1 ± 15.9 h; $p = 0.001$), mean time to tolerate diet (4.0 ± 0.8 *vs.* 5.0 ± 0.9 days; $p < 0.001$), mean length of hospital stay (5.9 ± 1. *vs.* 7.0 ± 1.4 days; $p < 0.001$) were significantly reduced in patients that received gum compared with controls.

In the absence of clinical and radiological signs of mechanical obstruction and abnormal laboratory exams suggesting peritonitis, all

**Table 1**
Clinical characteristics.

| | Control group (n = 75) | Gum group (n = 74) | *p* |
|---|---|---|---|
| Age (years)* | 55.4 ± 10.1 | 52.7 ± 11.2 | 0.13 |
| BMI (kg/m$^2$)* | 28.6 ± 4.5 | 28.1 ± 4.1 | 0.52 |
| Co-morbid disease** | 26 (34.7) | 17 (23.0) | 0.14 |
| Hypertension** | 16 (21.3) | 11 (14.9) | 0.39 |
| Diabetes mellitus** | 13 (17.3) | 10 (13.5) | 0.65 |
| Chronic pulmonary disease** | 2 (2.7) | 3 (4.1) | 0.68 |
| Cardiovascular disease** | 7 (9.3) | 4 (5.4) | 0.53 |
| Others†, ** | 5 (6.7) | 3 (4.1) | 0.71 |
| Indications for surgery** | | | 0.42 |
| Endometrial cancer | 41 (54.4) | 33 (44.6) | |
| Ovarian cancer | 26 (34.7) | 29 (39.2) | |
| Cervix cancer | 8 (10.7) | 12 (16.2) | |
| Previous abdominal surgery** | 14 (18.7) | 18 (24.3) | 0.43 |

Data are expressed as *: means ± standard deviation (SD) and **: (n %).
BMI, body mass index. †: Others = cholelithiasis, hepatitis.

**Table 2**
Operative characteristics.

| | Control group (n = 75) | Gum group (n = 74) | *p* |
|---|---|---|---|
| Number of removed LN* | | | 0.40 |
| Pelvic | 28.3 ± 5.3 | 27.6 ± 5.2 | |
| Para-aortic | 23.7 ± 4.9 | 24.7 ± 5.5 | |
| Hysterectomy** | | | 0.34 |
| Types 1–2 | 67 (89.3) | 62 (83.8) | |
| Type 3 | 8 (10.7) | 12 (16.2) | |
| Omentectomy** | | | 0.40 |
| No/biopsy | 24 (32.0) | 29 (39.2) | |
| Infracolic | 22 (29.3) | 15 (20.3) | |
| Total | 29 (38.7) | 30 (40.5) | |
| Appendectomy** | 3 (4.0) | 3 (4.1) | 1.00 |
| Douglas peritonectomy** | 4 (5.3) | 3 (4.1) | 1.00 |
| Extensive adhesiolysis** | 29 (38.7) | 31 (41.9) | 0.74 |
| Duration of operation (h)* | 2.9 ± 0.5 | 3.0 ± 0.6 | 0.25 |

Data are expressed as *: means ± standard deviation (SD); **: n (%).
LN, lymph nodes; CI, confidence interval.

**Table 3**
Postoperative clinical outcomes of the study groups.

| | Control group (n = 75) | Gum group (n = 74) | *p* | Relative risk (95% CI) |
|---|---|---|---|---|
| First flatus time (h)* | 43.6 ± 14.0 | 34.0 ± 11.5 | <0.001 | |
| First bowel movement time (h)* | 50.1 ± 15.9 | 41.5 ± 15.7 | 0.001 | |
| First defecation time (h)* | 62.5 ± 21.5 | 49.6 ± 18.7 | <0.001 | |
| Additional analgesic** | 8 (10.7) | 1 (1.4) | 0.03 | 7.8 (1.0–61.5) |
| Additional antiemetic** | 10 (13.0) | 2 (2.7) | 0.03 | 4.8 (1.0–21.1) |
| Ileus symptoms** | | | | |
| Mild | 27 (36.0) | 11 (14.9) | 0.004 | 2.4 (1.2–4.5) |
| Moderate | 8 (10.7) | 1 (1.4) | 0.03 | 7.8 (1.0–61.5) |
| Severe | 2 (2.7) | 0 | 0.49 | |
| Time to tolerate diet (d)* | 5.0 ± 0.9 | 4.0 ± 0.8 | <0.001 | |
| Length of hospital stay (d)* | 7.0 ± 1.4 | 5.9 ± 1.1 | <0.001 | |

Data are expressed as *: means ± standard deviation (SD); **: n (%).
CI, confidence interval; d, days; h, hours.

patients were successfully managed with conservative therapy, consisting of observation and basic support as the primary modality of approach. Mild symptoms have been observed in 27 (36.0%) patients in control group compared to 11 (14.9%) patients in gum group [relative risk (RR) 2.4; 95% confidence interval (CI), 1.2–4.5; p = 0.004]. All patients were treated by fasting, intravenous fluid administration to correct any underlying electrolyte abnormality and antiemetic drugs. Nine patients (eight in the control group and one in the gum group) were classified as moderate cases because they required the insertion of a nasogastric tube for gastric decompression. Severe symptoms were observed in two patients in the control group (2.7%), and neostigmine and magnesium oxide were arbitrarily used with success. No patients in either group required re-operation or readmission after hospital discharge.

## Discussion

This is the first trial to investigate the effect of postoperative gum chewing on bowel function after elective total abdominal hysterectomy and systematic retroperitoneal lymphadenectomy performed for complete staging of gynecological malignancies in the English literatures. The results demonstrated that gum chewing was associated with reduced time to the first flatus, defecation, and mean time of first bowel movement.

PI is a general term used to describe the absence of contractions in the intestines, which may be indicative of delayed return of physiological coordinated bowel motility, a major problem after abdominal surgery. It occurs most often after intra-abdominal surgery, but can also occur after retroperitoneal or even extra-abdominal surgery. The

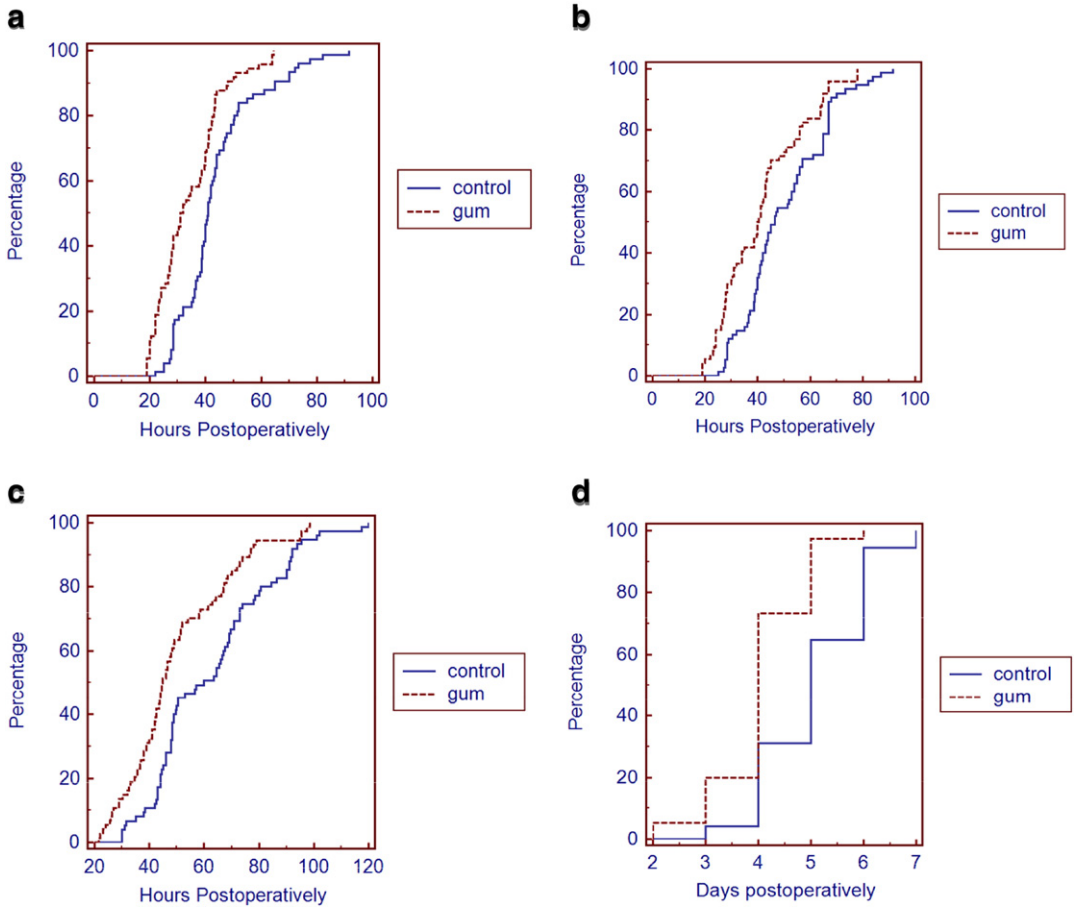


**Fig. 2.** Kaplan–Meier representations of (a) time to first passage of flatus, (b) time to first postoperative bowel movement, (c) time to first defecation, (d) time to tolerance diet.

etiology of PI remains controversial. Bowel motility is suppressed postoperatively owing to sympathetic hyperactivity and increased concentrations of circulating catecholamine [7]. Pacemaker dysfunction owing to bowel manipulation is another postulated mechanism of PI [8]. In addition, electrolyte abnormalities, peritoneal and/or retroperitoneal irritation, and narcotic analgesia effects may contribute to PI [10]. The focus of more recent studies has been on neural and humoral factors. Vasoactive intestinal peptide directly inhibits smooth muscle contraction in the intestine, and increased levels are seen after surgery [11]. In addition, pain increases the release of substance P, which is also known to inhibit bowel motility [12,13]. Surgery also inhibits the promotive hormones gastrin, neurotensin, and pancreatic polypeptide [8].

Recovery of gastrointestinal function is clinically important because PI is associated with increased postoperative pain, nausea, vomiting, prolonged hospital stays, and increasing both monetary and physiologic costs after abdominal surgery. In a recent meta-analysis of 17 prospective randomized trials that included 1347 patients, chewing gum significantly reduced recovery time following abdominal surgery. Patients in the chewing-gum-treatment group compared with the reference group experienced a significant reduction of 0.31 days for time to first flatus, 0.51 days for time to first bowel movement, 0.72 days for length of hospital stay [14].

In our study, the percentage of patients who experienced PI symptoms was higher in the control group than the gum-chewing group. Furthermore, more patients in the control group required additional analgesic agents. Our results showed that mean time to tolerate diet were shorter in the gum-chewing group. In addition, patients in the gum-chewing group were discharged earlier than those in the control group.

The mechanism behind reduced time to the first flatus, mean time of first bowel movement and of course PI symptoms with the use of chewing gum is unknown. Chewing a stick of gum may represent a form of 'sham feeding', whereby a food substance is chewed, but does not enter the stomach. Sham feeding may accelerate bowel function *via* a combination of mechanisms, including increased vagal cholinergic stimulation of the gut, which in turn leads to the release of gastrointestinal hormones such as gastrin, neurotensin and pancreatic polypeptide [15].

In the present study, the experimental and control groups were similar with respect to the factors that affect PI, including the systematic pelvic and para-aortic lymphadenectomy, incidence of appendectomy, the rate of douglas peritonectomy and extensive adhesiolysis, and mean duration of operation [16,17]. Another reason for the development of PI is whether the visceral peritoneum is closed. Although we did not close the visceral peritoneum in any of the patients in this study, this procedure is still under debate since some authors have reported that closure of either the parietal or visceral peritoneum is unnecessary [18].

No adverse effects have been reported after the use of chewing gum to stimulate sham feeding in patients after surgery [3–5,15,19–22]. Similarly in our trial, all patients in the intervention group were compliant with—and tolerant of—chewing gum, and there were no adverse events or complications related to the chewing gum.

The present study had several strengths, including that it was a large prospective randomized investigation, with similar demographic and surgical profiles and surgery performance by the same surgical team. However, there were also several limitations. First, we did not include a placebo comparison group, and it is not known whether a placebo effect may occur during evaluation of interventions for stimulation of bowel function. Matros et al. studied gum chewing and PI with two control groups; a no-gum group and an acupressure wrist bracelet placebo group. The no-gum group and acupressure bracelet group showed no differences in time to flatus and bowel movement, suggesting no placebo effect in studies of bowel motility [20]. Second, our study has a relatively small sample size for looking at parameters such as time to tolerate diet, additional analgesic and antiemetic requirement. For parameters such as time to tolerate diet, additional analgesic and antiemetic requirements, it is important to have pooled data from various trials to reach a powerful conclusion. Third, patients were not blinded; this may slightly reduce the effect of chewing gum. Finally, the most effective gum and the optimal amount of chewing remain unclear.

Despite these limitations, our findings indicate that gum chewing early in the postoperative period following elective total abdominal hysterectomy and systematic retroperitoneal lymphadenectomy hastens time to bowel motility and ability to tolerate feedings. This inexpensive and well-tolerated treatment resulted in earlier hospital discharge. We conclude that gum chewing should be added as an adjunct treatment in postoperative care of gynecologic oncology.

**Conflict of interest statement**

None of the authors has any conflict of interest relative to this work and this study did not receive pharmaceutical company support.

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