GYNECOLOGY

Effects of coffee consumption on gut recovery after surgery of gynecological cancer patients: a randomized controlled trial

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BACKGROUND: Paralytic ileus that develops after elective surgery is a common and uncomfortable complication and is considered inevitable after an intraperitoneal operation.

OBJECTIVE: The purpose of this study was to investigate whether coffee consumption accelerates the recovery of bowel function after complete staging surgery of gynecologic cancers.

STUDY DESIGN: In this randomized controlled trial, 114 patients were allocated preoperatively to either postoperative coffee consumption with 3 times daily (n=58) or routine postoperative care without coffee consumption (n=56). Total abdominal hysterectomy and bilateral salpingo-oophorectomy with systematic pelvic and paraaortic lymphadenectomy were performed on all patients as part of complete staging surgery for endometrial, ovarian, cervical, or tubal cancer. The primary outcome measure was the time to the first passage of flatus after surgery. Secondary outcomes were the time to first defecation, time to first bowel movement, and time to tolerance of a solid diet.

RESULTS: The mean time to flatus (30.2±8.0 vs 40.2±12.1 hours; $P<.001$), mean time to defecation (43.1±9.4 vs 58.5±17.0 hours; $P<.001$), and mean time to the ability to tolerate food (3.4±1.2 vs 4.7±1.6 days; $P<.001$) were reduced significantly in patients who consumed coffee compared with control subjects. Mild ileus symptoms were observed in 17 patients (30.4%) in the control group compared with 6 patients (10.3%) in the coffee group ($P=.01$). Coffee consumption was well-tolerated and well-accepted by patients, and no intervention-related side-effects were observed.

CONCLUSION: Coffee consumption after total abdominal hysterectomy and systematic paraaortic lymphadenectomy expedites the time to bowel motility and the ability to tolerate food. This simple, cheap, and well-tolerated treatment should be added as an adjunct to the postoperative care of gynecologic oncology patients.

Key words: coffee consumption, gynecologic cancer, ileus

Postoperative paralytic ileus (POPI) that develops after elective abdominal surgery is a common and uncomfortable complication that is considered inevitable after an intraperitoneal operation.[1] The incidence of POPI in patients who undergo pelvic and paraaortic lymphadenectomy (PPL) to treat gynecologic malignancies is 10.6−50%.[2,3] POPI contributes to patient discomfort, causes nausea, vomiting, and abdominal distension, and prolongs the hospital stay. This increases the risk for hospital-acquired infections, deep-vein thrombosis, and pulmonary compromise. POPI also increases hospital costs and the 30-day readmission rate.[4]

Despite the high incidence of ileus, preventative therapeutic options remain limited. Many efforts that include the administration of prokinetic compounds (such as serotonin receptor antagonists,[5] neostigmine,[6] alvimopam,[7] and ghrelin agonists[8]), early resumption of feeding,[9] gum chewing,[10] and adequate pain control[11,12] have been made to prevent ileus. Unfortunately, none of these strategies has been completely successful.[12]

Coffee is a popular drink worldwide and has various effects on medical conditions. Two reports have shown that coffee consumption after colectomy is both safe and associated with significantly faster resumption of intestinal motility.[13,14] Another study on the same topic remains ongoing.[15] However, no study has yet investigated the effects of coffee on gastrointestinal function in patients who have undergone surgery to treat gynecologic cancers, according to a systematic review of the literature (through PubMed, OvidSP, Google Scholar, and Scopus; Medline was searched from 1966 to July 2016 with the use of the following MeSH terms: ileus, coffee, gynecology). Thus, we explored the effects of coffee on postoperative bowel function in patients who had undergone either total or radical hysterectomy with bilateral salpingo-oophorectomy and systematic PPL to determine the stage of gynecologic cancers.

Materials and Methods

This randomized controlled study was conducted at the Tepecik Education and Research Hospital, Department of Gynecological Oncology, Izmir, Turkey, between November 2013 and February 2016. Ethical approval was obtained from the Istanbul Kanuni Sultan Suleyman Education and Research Hospital Ethics Committee (reference number: 10/2013). Additionally, the study was registered with clinicaltrials.gov (no. NCT01990482).

Patients who had received a diagnosis of cervical, endometrial, or ovarian cancer and scheduled for comprehensive staging surgery (abdominal hysterectomy and systematic PPL) were recruited. The exclusion criteria were any known

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hypersensitivity or allergy to caffeine/coffee, a thyroid disease, inflammatory bowel disease, compromised liver function, clinically significant cardiac arrhythmia, chronic constipation (defined as ≤2 bowel movements per week), a history of abdominal bowel surgery, previous abdominal irradiation, previous neoadjuvant chemotherapy or hyperthermic intraperitoneal chemotherapy, a need for intensive care for >24 hours postoperatively, a need for nasogastric tube drainage beyond the first postoperative morning, a bowel anastomosis, and the use of an upper abdominal multivisceral surgical approach for debulking surgery.

The study details were explained to all enrolled subjects. All participants gave written informed consent before inclusion in the trial. Randomization was performed when the patients were admitted to our gynecologic oncology clinic. Eligible patients were assigned randomly to 1 of 2 groups by a primary investigator (K.G.) who consecutively opened sequentially numbered, opaque, sealed envelopes. Caffeine and nicotine consumptions were recorded. Envelope randomization was performed with the use of a computer-generated code running a blocked randomization protocol. Group A served as the control group and received no treatment; group B (the coffee group) drank 3 cups of caffeinated coffee daily (100 mL at 10:00 AM, 3:00 PM, and 7:00 PM), beginning on the morning after surgery. Patients were asked to drink the entire 150-mL amounts within 20 minutes under the supervision of a nurse or doctor. Patients were free to drink any amount of water but no more coffee, black tea, or other form of caffeine, such as soda. Coffee was prepared with a conventional coffee machine (Nescafe Alegria; 100 g caffeine; Nestlé. Gatwick, United Kingdom).

After enrollment, we implemented a standard clinical protocol. Before operations, all patients who were scheduled for comprehensive staging surgery ingested a clear liquid diet and underwent mechanical bowel preparation with 20 g MgO (Magnesi-Kalsine Toz; İstanbul İlaç, Istanbul, Turkey) and 28.5 g NaH_2P with 10.5 g Na_2HP (BT Enema; Yenisehir Laboratory, Ankara, Turkey), low-molecular-weight heparin, and prophylactic intravenous antibiotics at the time of induction of anesthesia. All patients underwent the same anesthetic protocol (in general, propofol and Tracrium were administered intravenously, and sevoflurane and nitrous oxide were administered by inhalation with epidural catheter analgesia).

All patients underwent total abdominal hysterectomy with systematic PPL as part of their staging procedures. All operations were performed by the same surgical team. Our postoperative care protocol featured the administration of the prokinetic agent metoclopramide (as an antiemetic), if required, and prophylaxis for stress-induced gastritis in the form of histamine H_2 blockers for 48 hours after surgery. All patients received steady oral paracetamol for 48 hours after operation, after removal of the epidural catheter. Additional nonsteroidal analgesia was provided when required, and its use was carefully documented. Antiemetic agents were prescribed for nausea, if required. No opioid antagonists were used postoperatively. Early ambulation was encouraged; all patients were mobilized after assuming a sitting position in bed for 10 minutes to prevent hypotension, starting from 24 hours after surgery; patients walked approximately 5−10 meters. The postoperative feeding regime was standardized; a liquid diet was begun on the first postoperative day and progressed to a regular diet within the next 24 hours, as tolerated.

The defined primary outcome measure was the time to the first passage of flatus after surgery. The secondary outcomes were the time to first defecation, time to first bowel movement, time to toleration of a solid diet, any potential side-effects of postoperative coffee intake, whether antiemetics were needed on the morning after surgery, whether analgesics in addition to those used in our clinic routine were required, POPI type and rate, and the length of hospital stay.

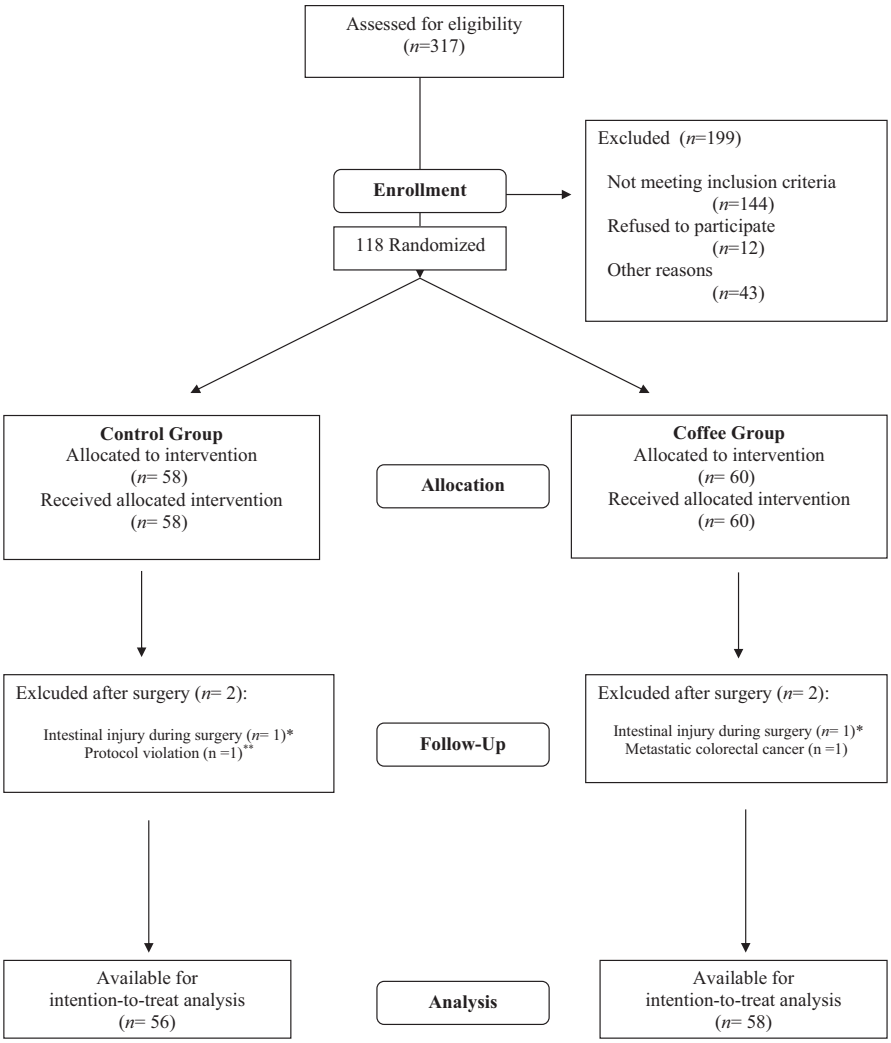
The time to tolerance of a solid diet was measured from the end of surgery (defined as when the patients woke up from anesthesia) until the patient tolerated the intake of solid food (any food that required chewing) without vomiting or experiencing significant nausea within 4 hours after the meal and without reversion to enteral fluids only. The time to the first bowel movement was defined as the time to the first audible bowel sound during routine postoperative treatment.

POPI was considered to be resolved after the first passage of flatus if abdominal distension and vomiting were both absent. The symptoms were categorized as *mild* if they resolved spontaneously within a few days with only observation and basic support, *moderate* if vomiting persisted and reinsertion of the nasogastric tube was clinically required, and *severe* if symptoms persisted for >2 days or resisted treatment.[10]

The symptoms and signs of ileus were evaluated 3 times daily by an evaluator who was blinded to the study allocation. To monitor the recovery of bowel function precisely, patients were instructed to notify ward nurses or investigators immediately after the first occurrence of flatus, bowel movement, or defecation. We also checked all bowel sounds 6 times daily.

Unfortunately, complete blinding after the assignment of the interventions could not be achieved because of the nature of the study. The hospital discharge criteria were stable vital signs with no fever (defined as body temperature ≥38.5°C) for at least 24 hours, the ability to ambulate without assistance, the ability to tolerate solid food without vomiting, normal urination and defecation, and the absence of any complications after surgery.

FIGURE
Flow diagram of trial recruitment and follow-up evaluation



The single asterisk indicates that intestinal injuries happened intraoperatively; the double asterisks indicate that 1 patient drank a cup of black tea on the first postoperative day.

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At the start of the trial, all studies to date that had explored coffee intake had included only patients who had undergone colonic surgery. Thus, we ran a nonblinded pilot trial of 20 patients in each group (A and B) before the full trial. The mean time to flatus was 43.7±13.3 hours in group A and 31.7±6.9 hours in group B. Based on these data, we calculated that, to attain a study power of 90% with an α level of .05, 49 patients were required in each group. Assuming a 20% dropout rate, 118 patients were required.

Whether variables were distributed normally was examined with the use of the Kolmogorov-Smirnov test. The χ^2 and Fisher's tests were used to compare categoric variables; the Student *t* test was used to compare normally distributed continuous variables, and the Mann-Whitney *U* test was used to compare variables that were not normally distributed. Odds ratios were estimated with the use of Cox's proportional hazard modeling. Statistical analyses were performed with the use of Med Calc (version 16.4; Ostend, Belgium). We used an intention-to-treat protocol. A probability value of <.05 was considered significant.

Results

During the study period, in total, 118 patients were enrolled; 60 patients were assigned randomly to the coffee group, and 58 were assigned to the control group. Four patients (2 in the control group and 2 in the treatment group) were excluded after randomization because they no longer fulfilled the inclusion criteria. Ultimately, the conditions of 56 patients in the control group and 58 in the coffee group were analyzed. The reasons for exclusion before and after randomization are shown in the Figure. The patient characteristics of each group were comparable and are shown in Table 1. In both groups, endometrial cancer (50.0% in the control vs 55.2% in the coffee group) was the most common indication for comprehensive staging surgery.

The types of operative procedures for both the coffee and control groups are shown in Table 2. Two patients (3.6%) in the control group and 4 patients (6.9%) in the coffee group underwent type III radical hysterectomy and systematic pelvic lymphadenectomy and paraaortic lymphadenectomy up to the inferior mesenteric artery to treat cervical carcinoma. The durations of operations were similar between the groups (P=.63). Metoclopramide 10 mg was used by 15 patients (28.8%) patients in the control group and by 10 patients (17.2%) in the coffee group (P=.15).

Coffee consumption was well-tolerated by all patients. Furthermore, no adverse events were observed in the context of coffee intake. The primary and secondary outcomes of the study are shown in Table 3. The mean time to first flatus was shorter in the coffee group than in the control group (29.7±4.9 vs 41.6±10.9 hours; P<.001). In addition, the time to first defecation was significantly shorter in the coffee group (42.0±6.8 vs 59.8±14.6 hours; P<.001), as was the time until patients could tolerate food (3.5±1.2 vs 4.8±1.6 days; P<.001).

TABLE 1
Baseline characteristics of the patients

Characteristic	Control group (n=56)	Coffee group (n=58)	*P* value
Age, y[a]	53.1±11.4	56.6±10.1	.09
Body mass index, kg/m^2[a]	27.4±3.6	27.9±4.1	.48
Gravida[a]	2.3±1.0	2.5±1.4	.26
Tobacco use, n (%)	4 (7.1)	6 (10.3)	.74
Ethanol use, n (%)	1 (1.8)	—	.49
Coffee drinker, n (%)	12 (21.4)	14 (24.1)	.73
Hypertension, n (%)	8 (14.3)	12 (20.7)	.46
Diabetes mellitus, n (%)	7 (12.5)	9 (15.5)	.78
Cardiovascular disease, n (%)	2 (2.6)	3 (5.2)	1.00
Other comorbid disease, n (%)	5 (8.9)	4 (6.9)	.74
Indication for surgery, n (%)			.69
Endometrial cancer	28 (50.0)	32 (55.2)	
Ovarian cancer	24 (42.9)	21 (36.2)	
Cervical cancer	2 (3.6)	4 (6.9)	
Fallopian tube cancer	2 (3.6)	1 (1.7)	
Previous abdominal surgery, n (%)	9 (16.1)	11 (19.0)	.80

[a] Data are given as mean±standard deviation.

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TABLE 2
Surgical characteristics of the patients

Characteristic	Control group (n=56)	Coffee group (n=58)	*P* value
Hysterectomy type[a], n (%)			.37
I	45 (80.4)	49 (84.5)	
II	9 (16.1)	5 (8.6)	
III	2 (3.6)	4 (6.9)	
No. of removed lymph node[b]			
Pelvic	24.6±10.6	26.8±10.5	.25
Paraaortic	21.3±9.8	20.6±7.7	.69
Omentectomy, n (%)	40 (71.4)	39 (67.2)	.62
Peritonectomy, n (%)	8 (14.3)	10 (17.2)	.79
Appendectomy, n (%)	3 (5.4)	5 (8.6)	.71
Duration of operation, min[b]	196.7±47.6	200.5±34.0	.63
Duration of anesthesia, min[b]	218.4±47.1	222.6±35.2	.58
Blood transfusion, n (%)	5 (8.9)	4 (6.9)	.74

[a] According to reference 23; [b] Values are mean ± standard deviation.

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In patients with no clinical or radiologic signs of mechanical obstruction and abnormal laboratory results that supported peritonitis, conservative therapy was successful and primarily consisted of observation and basic support. Mild symptoms were seen in 17 patients (30.4%) in the control group compared with 6 patients (10.3%) in the coffee group. All patients were treated by fasting, intravenous fluid administration to correct any underlying electrolyte abnormality, and antiemetic pills. Nine patients in the control group and 2 patients in the coffee group required the insertion of nasogastric tubes to allow gastric decompression; they were classified as having moderate POPI. Octreotide, erythromycin, and neostigmine were given arbitrarily, without success, to 3 patients in the control group who had severe POPI symptoms. No patients required readmission or reoperation after hospital discharge. Patients' conditions were analyzed according to POPI (Table 4). Patients who drank coffee after surgery were less likely to have POPI (21.6% vs 64.9%; $P<.001$). Furthermore, coffee consumption during the postoperative period independently protected against the development of POPI (Table 5).

Comment

This randomized trial showed that coffee consumption during the early postoperative period after abdominal hysterectomy and systematic PPL shortened the time to bowel motility and the ability to tolerate food. Moreover, a regression model showed that coffee consumption after surgery was independently protective against the development of POPI. It has a low cost, compared with pharmacologic management to prevent ileus (such as opioid receptor antagonists, ghrelin receptor agonists, and serotonin receptor agonists). Additionally, it is simple and well-tolerated and results in cost savings by reducing the length of the hospital stay.

Although POPI is usually self-resolving, it is a clinically and economically important consequence of major abdominal surgery. The pathophysiologic condition of POPI is poorly defined and multifactorial; the key contributory factors include induction of an inflammatory response, the effects of surgical manipulation, administration of opioids, autonomic dysfunction, and disturbances in gastrointestinal hormone activity and electrolyte fluctuations.[16] Unfortunately, the therapeutic options for the prevention of ileus remain limited.

The English-language literature includes only 2 studies that have explored whether coffee consumption may reduce POPI.[13,14] Müller et al[13] randomly assigned 80 patients to receive either coffee or warm water after elective colectomy. The coffee drinkers experienced significantly shorter times to the first bowel movement and tolerance of solid food. The time to first flatus was also shorter in the coffee-drinker arm, but the difference was not statistically significant. Likewise, Dulskas et al[14] studied patients who had undergone elective colectomy and found similar results, although the time to first flatus was significantly shorter in the coffee drinkers.

In the present study, POPI symptoms were more common in the control group than in the coffee group. Furthermore, the need for additional analgesics and/or antiemetics was significantly lower in the coffee group. This may be attributable to reductions in bloating and distension that are caused by accelerated passage of the first flatus. In addition, patients who drank coffee were discharged earlier than patients in the control group. Our results may be very useful as a reference when gynecologic cancer surgery is considered. Systematic PPL is used commonly in the staging and treatment of primary gynecologic tumors. Lymphadenectomy, particularly when performed in the paraaortic area, further increases the risk for POPI during staging surgery.[17]

TABLE 3
Study outcomes

Outcome	Control group (n=56)	Coffee group (n=58)	*P* value
Mean time of first flatus, hr[a]	41.6±10.9	29.7±4.9	<.001
Mean time of first bowel movement, hr[a]	47.5±11.7	35.6±5.4	<.001
Mean time of first defecation, hr[a]	59.8±14.6	42.0±6.8	<.001
Additional analgesic, n (%)	10 (17.9)	2 (3.4)	.01
Additional antiemetic, n (%)	9 (16.1)	2 (3.4)	.02
Ileus symptoms, n (%)	29 (51.8)	8 (13.8)	<.001
Mild	17 (30.4)	6 (10.3)	.01
Moderate	9 (16.1)	2 (3.4)	.02
Severe	3 (5.4)	—	.11
Time to tolerate diet, d[a]	4.8±1.6	3.5±1.2	<.001
Length of hospital stay, d[a]	7.4±2.9	6.1±1.1	.003

[a] Values are means ± standard deviation.

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Regarding the mechanisms that might explain our results, coffee is a very popular beverage, and its effects on general well-being, the central nervous system, and the cardiovascular system are well-known.[18,19] Its effects on the gastrointestinal tract are probably not only attributable to its physicochemical properties (caloric content, volume load, acidity, and osmolarity), which stimulate the gastrointestinal system, but also to the biochemical activities of ≥1 of the many compounds in coffee. Coffee increases colonic motor activity within 4 minutes after ingestion.[20,21] Caffeine is the most popular and

TABLE 4
Patients' demographic and clinical characteristics, according to the presence or absence of postoperative ileus symptoms (POPI)

Variable	Postoperative ileus symptoms, n (%)		*P* value
	Patients without (n=77)	Patients with (n=37)	
Age ≥60 y	30 (39.0)	10 (27.0)	.21
Body mass index ≥30 kg/m^2	21 (27.3)	14 (37.8)	.25
Coffee drinker	21 (27.3)	5 (13.5)	.15
Tobacco user	5 (6.5)	5 (13.5)	.28
Previous abdominal surgery	11 (14.3)	9 (24.3)	.19
Hysterectomy types II & III[a]	5 (6.5)	15 (40.5)	<.001
Omentectomy	48 (62.3)	31 (83.8)	.02
Peritenectomy	6 (7.8)	12 (32.4)	.002
Metoclopramide use	15 (19.5)	10 (27.0)	.46
Coffee consumption after the surgery	50 (64.9)	8 (21.6)	<.001

[a] According reference 23.

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TABLE 5
Univariate and multivariate analyses of the risk factors for postoperative paralytic ileus

	Univariate analysis			Multivariate analysis		
Variable	Relative risk	95% Confidence interval	*P* value	Relative risk	95% Confidence interval	*P* value
Age (<60 vs ≥60 y)	1.6	0.7–3.3	.30	1.3	0.5–3.1	.48
Coffee drinker before surgery	0.5	0.2–1.3	.18	0.7	0.2–1.9	.52
Body mass index (<30 vs ≥30 kg/m^2)	1.3	0.7–2.6	.34	1.3	0.6–2.7	.41
Peritenectomy (yes/no)	2.5	1.2–5.0	.007	1.8	0.8–3.9	.13
Hysterectomy type[a] (I vs II and III)	3.2	1.6–6.1	.005	2.8	1.2–6.4	.01
Omentectomy (yes/no)	2.2	0.9–5.4	.06	1.9	0.7–4.8	.15
Previous abdominal surgery	1.5	0.7–3.2	.29	1.3	0.5–3.0	.49
Metoclopramide use	1.3	0.6–2.7	.45	0.6	0.2–1.4	.27
Coffee consumption after surgery	0.2	0.1–0.5	.0009	0.2	0.1–0.6	.001

[a] According to reference 23.

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well-known component of coffee; it antagonizes the adenosine receptors that inhibit gastrointestinal motility and thus may be the component that stimulates the bowel.[22] However, Dulskas et al[14] reported a shorter time to first bowel movement with decaffeinated coffee, compared with coffee with caffeine. This may be explained by the formation of new chemically active components during decaffeination. Unfortunately, the mechanisms by which coffee stimulates intestinal motility remain largely unclear. In our study, the groups were similar in terms of the factors that cause POPI, which include the number of removed pelvic and paraaortic lymph nodes, the incidences of peritonectomy, the rates of appendectomy, and the mean operation times.[17]

No study to date has reported any adverse effects after coffee consumption during the postoperative period.[13,14] Similarly, all patients in the intervention arm of our study were compliant with and tolerated coffee consumption; we recorded no adverse events or complications that were related to coffee consumption.

Our study had several strengths, which include the fact that it was a prospective randomized investigation and that the 2 groups had similar demographic and surgical profiles. Moreover, the fact that the investigation was performed at a single institution by the same team of surgeons probably increases the validity of our results. On the other hand, the study had several limitations. First, we did not have a placebo group; thus, we do not know whether there were any placebo effects. Second, the patients were not blinded; this may have affected the effects of coffee to a small extent. Third, the best type of coffee (with or without caffeine) and the optimal amount remain unclear. Fourth, when parameters such as additional analgesic and antiemetic requirements and the potential adverse effects of coffee are being evaluated, it is important to pool data from various trials to strengthen the conclusions. Fifth, the hospital stay durations were relatively long in our study, compared with European hospital policies. However, our hospital is a tertiary center for gynecologic oncology in the Aegean region, and many patients visit our clinic from distant locations. In addition, social issues sometimes rendered it necessary to prolong the hospital stays beyond those required by medical necessity. Despite these limitations, we conclude that coffee consumption after complete staging surgery for gynecologic malignancies is beneficial for the prevention of POPI. The cost is low compared with pharmacologic management to prevent ileus, and it should be used as an adjunct treatment during postoperative care. ■

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References

1. Lubawski J, Saclarides TJ. Postoperative ileus: strategies for reduction. Ther Clin Risk Manag 2008;4:913-7.
2. Fujita K, Nagano T, Suzuki A, et al. Incidence of postoperative ileus after paraaortic lymph node dissection in patients with malignant gynecologic tumors. Int J Clin Oncol 2005;10:187-90.
3. Tabata T, Kihira T, Shiozaki T, et al. Efficacy of a sodium hyaluronate-carboxycellulose membrane (Seprafilm) for reducing the risk of early postoperative small obstruction in patients with gynecologic malignancies. Int J Gynecol Cancer 2010;20:188-93.
4. Johnson MD, Walsh RM. Current therapies to shorten postoperative ileus. Cleve Clin J Med 2009;76:641-8.
5. Toyomasu Y, Mochiki E, Morita H, et al. Mosapride citrate improves postoperative ileus of patients with colectomy. J Gastrointest Surg 2011;15:1361-7.
6. Drake TM, Ward AE. Pharmacological management to prevent ileus in major abdominal surgery: a systematic review and meta-analysis. J Gastrointest Surg 2016;20:1157-72.
7. Tan EK, Cornish J, Darzi AW, Tekkis PP. Meta-analysis: alvimopan vs placebo in the treatment of post-operative ileus. Aliment Pharmacol Ther 2007;25:47-57.
8. Beck DE, Sweeney WB, McCarter MD. Prospective, randomized, controlled, proof-of-

concept study of the Ghrelin mimetic ipamorelin for the management of postoperative ileus in bowel resection patients. Int J Colorectal Dis 2014;29:1527-34.
9. Zhuang CL, Ye XZ, Zhang CJ, Dong QT, Chen BC, Yu Z. Early versus traditional postoperative oral feeding in patients undergoing elective colorectal surgery: a meta-analysis of randomized clinical trials. Dig Surg 2013;30:225-32.
10. Ertas IE, Gungorduk K, Ozdemir A, Solmaz U, Dogan A, Yildirim Y. Influence of gum chewing on postoperative bowel activity after complete staging surgery for gynecological malignancies: a randomized controlled trial. Gynecol Oncol 2013;131:118-22.
11. Wongyingsinn M, Baldini G, Charlebois P, Liberman S, Stein B, Carli F. Intravenous lidocaine versus thoracic epidural analgesia: a randomized controlled trial in patients undergoing laparoscopic colorectal surgery using an enhanced recovery program. Reg Anesth Pain Med 2011;36:241-8.
12. Bragg D, El-Sharkawy AM, Psaltis E, Maxwell-Armstrong CA, Lobo DN. Postoperative ileus: recent developments in pathophysiology and management. Clin Nutr 2015;34:367-76.
13. Müller SA, Rahbari NN, Schneider F, et al. Randomized clinical trial on the effect of coffee on postoperative ileus following elective colectomy. Br J Surg 2012;99:1530-8.
14. Dulskas A, Klimovskij M, Vitkauskiene M, Samalavicius NE. Effect of coffee on the length of postoperative ileus after elective laparoscopic left-sided colectomy: a randomized, prospective single-center study. Dis Colon Rectum 2015;58:1064-9.
15. Kruse C, Müller SA, Warschkow R, et al. Does caffeine reduce postoperative bowel paralysis after elective laparoscopic colectomy? (CaCo trial): study protocol for a randomized controlled trial. Trials 2016;17:186.
16. Vathe R, O'Grady G, Bissett IP, Dinning PG. Postoperative ileus: mechanisms and future directions for research. Clin Exp Pharmacol Physiol 2014;41:358-70.
17. Fagotti A, Fanfani F, Ercoli A, Giordano MA, Sallustio G, Scambia G. Postoperative ileus after para-aortic lymphadenectomy: a prospective study. Gynecol Oncol 2007;104:46-51.
18. Lane JD, Adcock RA, Williams RB, Kuhn CM. Caffeine effects on cardiovascular and neuroendocrine responses to acute psychosocial stress and their relationship to level of habitual caffeine consumption. Psychosom Med 1990;52:320-36.
19. Robertson D, Frölich JC, Carr RK, Oates JA. Effects of caffeine on plasma renin activity, catecholamines and blood pressure. N Engl J Med 1978;298:181-6.
20. Brown SR, Cann PA, Read NW. Effect of coffee on distal colon function. Gut 1990;31:450-3.
21. Rao SSC, Welcher K, Zimmerman B, Stumbo P. Is coffee a colonic stimulant? Eur J Gastroenterol Hepatol 1998;10:113-8.
22. Boekema PJ, Samsom M, van Berge Henegouwen GP, Smout AJ. Coffee and gastrointestinal function: facts and fiction: a review. Scand J Gastroenterol Suppl 1999;230:35-9.
23. Piver MS, Rutledge F, Smith JP. Five classes of extended hysterectomy for women with cervical cancer. Obstet Gynecol 1974;44:265-72.

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