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Effect of Caffeine Intake on Postoperative Ileus: A Systematic Review and Meta-Analysis

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Keywords
Caffeine · Coffee · Postoperative ileus · Enhance recovery · Intestinal paralysis

Abstract
Background: Postoperative ileus prolongs both hospital stay and patients' morbidity, having at the same time a great impact on health care costs. Coffee, a worldwide popular, cheap beverage might have an important effect on the motility of the postoperative bowel. ***Methods:*** PubMed, Scopus, and Cochrane Central Register of Controlled Trials were systematically searched. ***Results:*** Four studies met the inclusion criteria of our meta-analysis. A total of 341 patients were included. The postoperative administration of coffee significantly reduces the time to first bowel movement, the time to first flatus and the time to tolerance of solid diet. Safe conclusions could not be drawn regarding the additional use of laxatives, the necessity for reinsertion of nasogastric tube or the need for reoperation as all the aforementioned outcomes did not present any statistically significance. None of the complications were attributed to the administration of coffee. ***Conclusion:*** The administration of coffee as a postoperative ileus prevention measure can change the way postoperative enhanced recovery is applied. Even though the mechanism of action of coffee is not fully known, currently available literature demonstrates a significant improvement in gastrointestinal motility without having any impact on postoperative morbidity. Studies with higher methodological quality can offer a more careful evaluation of the clinical use of this popular beverage.

Introduction

Postoperative ileus is the bowel paralysis that is observed in the postoperative period after abdominal surgery [1, 2]. The incidence of this type of paralytic ileus, in the literature, ranges between 10 and 30% [3, 4]. This postoperative delayed recovery of physiological gastrointestinal motility is often self-resolving [5]. However, the prolonged hospital stays and morbidity resulting from postoperative ileus have a great impact on health care costs [6, 7]. It has been shown that postoperative ileus causes an increase in hospital spending of USD 750 million/year [1, 8].

In clinical practice, postoperative ileus is characterized by nausea, vomiting, intestinal cramps, abdominal distension and patient discomfort [1]. Initially this type of

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ileus is treated through nasogastric tube decompression, correction of electrolyte imbalances and analgesia when needed [9, 10]. In addition, in order to reduce the incidence of postoperative ileus, various preventive strategies have been tried. Multimodal approaches both in the surgical technique and the postoperative treatment have been used without complete success [11]. However, in order to minimize the incidence of postoperative ileus, a number of enhanced recovery protocols in various surgical fields have been proposed [12–17].

Coffee is a worldwide popular beverage, which has multiple effects on the human body. The ones that have been most frequently documented are those of the central nervous system and the cardiovascular system [18, 19]. However, existing evidence on the effect of coffee on the gastrointestinal system, and especially on that of the postoperative bowel, can be considered limited [20, 21].

In this study, we sought to present the available evidence concerning the postoperative administration of coffee in enhanced recovery in the postoperative period, by performing a systematic review of the current literature.

Methods

Data Sources

A systematic, electronic search was performed in PubMed, Scopus and Cochrane Central Register of Controlled Trials. All databases were assessed up to December 20, 2017. The search strategy utilized in all databases; it included a combination of the key words: (coffee OR caffeine) AND (bowel paralysis OR recovery OR paralytic ileus OR ileus). A hand-search was also performed, in the references of relevant articles, for additional studies.

Study Selection Criteria

Studies reporting data on the postoperative administration of coffee in order to enhance postoperative recovery was included in this review. Abstracts in scientific conferences, editorials as well as animal studies were not included in the study. Studies published in languages other than English, Spanish, German, French, Italian or Greek were excluded from this review. Only randomized control trials were included for further analysis.

Definitions

Estimated blood loss was the blood loss during the procedure and was usually obtained from both the anaesthesia records and/or the surgeons' operative reports. Complications included all the events associated with the administration of coffee and were defined by specific criteria that were present in the individual included studies. However, major complications such as anastomotic leakage or death were not included in the definition.

Statistical Considerations

Pooled estimations regarding clinical outcomes expressed either as dichotomous or continuous variables were calculated with the utilization of a random effect model. More specifically, we estimated the pooled mean difference to assess continuous data, while pooled ORs were calculated for the assessment of dichotomous data. Statistical heterogeneity between the included studies was assessed with the chi-square test and I^2. All statistical analyses were performed by using the Review Manager Version 5.2 software (The Nordice Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark, 2012). A p value of <0.05 was considered statistically significant.

Quality Assessment of the Included Studies

Quality assessment of the included studies was performed by applying the Jadad score [22]. In accordance with the Jadad score, 5 is the maximum score that can be assigned to a trial. Additionally, 1 point could be assigned to a study if it was randomized blinded and reported information regarding withdrawal respectively. One point was also assigned to a trial when the randomization and blinding procedures were considered appropriate. The proper long-term follow-up of the included patients was also evaluated (1 point). Scores superior to 2 points were considered to denote a study of adequate quality [23]. Discrepancies as far as the quality assessment of the included studies were assessed by consulting an extra party.

Results

Selected Studies

During the performed search in PubMed, Scopus and Cochrane databases a total of 1,061, 53 and 129 search results, respectively, were retrieved of which 4 studies (4 randomized controlled studies) were identified as eligible for inclusion in our review. No additional studies were identified through hand-searching of references. The included studies are graphically represented in Figure 1.

Characteristics of the Included Studies

The main characteristics of the studies included in our review (Jadad score, intention to treat population, age of patients, type of operation, previous abdominal surgery, duration of operation, estimated blood loss, type of anastomosis, blood transfusions, permanence in intensive care unit, presence of complications) are presented in Table 1.

The literature search revealed 4 randomized control studies [5, 24–26]; 3 studies referred to colorectal procedures, while only one study referred to gynaecological surgery [25]. In total, 341 patients were included. The sample size of the individual studies varied considerably (minimum 58, maximum 114 patients). Coffee was administered postoperatively to 156 patients. Only one study mentioned the presence of prior abdominal surgery

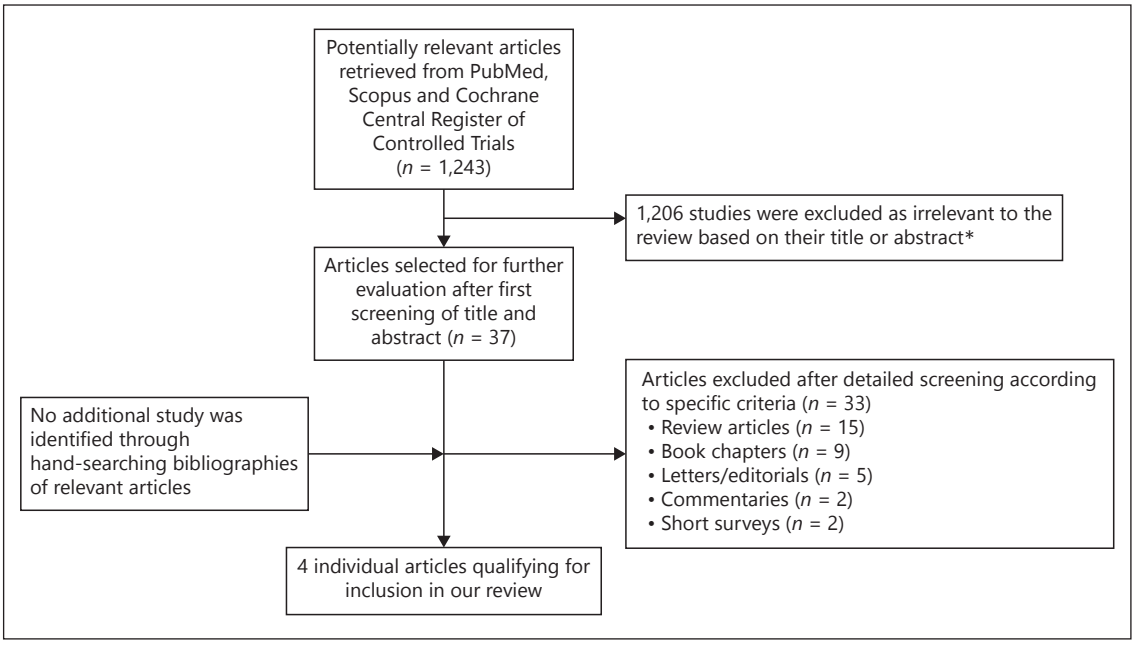

Fig. 1. Flow diagram of the selection process of articles included in the review.

(p = 0.8). Two studies reported perioperative management as per fast-track surgery [5, 24]. However, neither of these studies reported on treatment an improvement in postoperative bowel motility.

In addition, 3 out of the 4 included studies reported on the use of laxative. Detailed data from the included trials regarding outcomes of the meta-analysis is presented in Table 2.

Outcomes

Use of Laxatives

Two studies were included in the analysis regarding the need for laxatives in order to promote intestinal motility [5, 26]. No statistically significant difference was observed between the compared groups in the included studies (137 patients, OR 0.71; 95% CI 0.23–2.19; Fig. 2).

Reinsertion of Nasogastric Tube

Four studies provided data regarding the necessity of reinsertion of nasogastric tube during the recovery period [5, 24–26]. No statistically significant difference was observed between the compared groups (311 patients, OR 0.56; 95% CI 0.19–1.62; Fig. 2).

Need of Reoperation

Two studies were included in the analysis regarding the need for reoperation [5, 26]. No statistically significant difference was observed between the compared groups (137 patients, OR 0.41; 95% CI 0.07–2.37; Fig. 2).

Complications

Data regarding the presence of complications was provided by 3 studies [5, 24, 26]. The administration of coffee during the postoperative period did not significantly increase complications when compared to the control group (197 patients, OR 0.44; 95% CI 0.16–1.21; Fig. 2).

Time to First Bowel Movement

Two studies provided data regarding the time period till the first bowel movement [5, 25]. The mean difference observed between the compared groups was statistically significant with p value of <0.001, in favour of the coffee group (12.09 h, 95% CI 8.92–15.26; Fig. 3).

Time to Tolerance of Solid Food

Two studies provided data regarding the time to tolerance of solid food [5, 25]. A statistically significant difference (p < 0.001) was observed between the compared groups, favouring the coffee group (1.31 h, 95% CI 0.79–1.83; Fig. 3).

Time to First Flatus

Data regarding the time to first flatus was provided by 2 studies [5, 25]. The mean difference observed between

Table 1. Characteristics of the included studies regarding the coffee consumption on postoperative recovery

First author, year, country [Ref]	Jadad score	ITT population	Age of patients, years	Type of operation	Previous abdominal surgery, %	Duration of operation, min	Estimated blood loss, mL	Type anastomosis (S/M)	Blood transfusions	Stay in ICU
Coffee [n_1/N_1, (%)] vs. Control [n_2/N_2, (%)]										
Güngördük, 2016, Turkey [25]	3	58 vs. 56*	Mean (SD): 56.6 (10.1) vs. 53.1 (11.4), $p = 0.09$	Hysterectomy 58 vs. 56, Omentectomy 39 vs. 40, Peritonectomy 10 vs. 8 Appendectomy 5 vs. 3	11 vs. 9, $p = 0.8$	Mean (SD): 200.5 (34) vs. 196.7 (47.6), $p = 0.63$	NM	–	4 vs. 5, $p = 0.74$	NM
Dulskas, 2015, Lithuania [24]	3	30 vs. (DC: 30 vs. W: 30)	Median (SD): 67.3 (6.8) vs. 62.4 (10.8) vs. 66.3 (9.1), $p = 0.887$	Anterior rectal resection 11 vs. 12 vs. 9, $p = 0.765$ Left hemicolectomy 7 vs. 5 vs. 5, $p = 0.891$ Sigmoidectomy 12 vs. 13 vs. 16, $p = 0.456$	NM	Median (SD): 102 (37.2) vs. 103 (42.5) vs. 98 (35.2), $p = 0.465$	NM	NM	NM	NM
Piric, 2015, Bosnia and Herzegovina [26]	2	28 vs (T: 30)	Mean (SD): 63.6 (2) vs. 62.7 (3.1)	Anterior rectal resection 7 vs. 4 Left hemicolectomy 6 vs. 9 Right hemicolectomy 5 vs. 15, $p < 0.05$ Sigmoidectomy 10 vs. 2, $p < 0.01$	NM	Mean (SD): 139.3 (6.8) vs. 130.8 (6.8), $p < 0.05$	NM	M: 6/28 (21.4) vs. 19/30 (63.3) S: 22/28 (78.6) vs. 11/30 (36.7)	16/28 (57) vs. 18/30 (60), $p < 0.05$	9/28 (32.1) vs. 9/30 (30), $p < 0.05$
Müller, 2012, Switzerland [5]	3	40 vs. (W: 39)	Mean (SD): 62 (12) vs. 59 (15)	Ileocaecal resection 4/40 (10) vs. Left hemicolectomy 4/40 (10) vs. 5/39 (13) Right hemicolectomy 11/40 (28) vs. 15/39 (38) Sigmoidectomy 21/40 (53) vs. 13/39 (33), p = 0.392	NM	Mean (SD): 173 (56) vs. 183 (57), $p = 0.41$	Mean (SD): 150 (87) vs. 202 (211), $p = 0.48$	NM	3/40 (8) vs. 7/39 (18), $p = 0.16$	7/40 (18) vs. 8/39 (21), $p = 0.73$

* Received no treatment.
ITT, intention to treat; NM, not mentioned; N, number; S, stapled; M, manual; ICU, intensive care unit; DC, decaffeinated coffee; W, water; T, tea.

Table 2. Extracted data from the included randomized controlled trials regarding outcomes of meta-analysis

First author, year, country [Ref]	Time to first bowel movement, h	Time to tolerance of solid food, h	Time to first flatus, h	Time of first defecation, h	Use of any laxatives	Reinsertion of nasogastric tube	Complications, %	Reoperation	Length of hospital stay, days
Coffee [n_1/N_1, (%)] vs Control [n_2/N_2, (%)]									
Güngördük, 2016, Turkey [25]	Mean (SD): 35.6 (5.4) vs. 47.5 (11.7), $p < 0.001$	Mean (SD): 3.5 (1.2) vs. 4.8 (1.6), $p < 0.001$	Mean (SD): 29.7 (4.9) vs. 41.6 (10.9), $p < 0.001$	Mean (SD): 42 (6.8) vs. 59.8 (14.6), $p < 0.001$	NM	2/58 (3.4) vs. 9/56 (16.1), $p = 0.02$	NM	NM	Mean (SD): 6.1 (1.1) vs. 7.4 (2.9), $p = 0.003$
Dulskas, 2015, Lithuania [24]	Median (range): 3.75 (1.53) vs. 3 (1.5) vs. 4.14 (1.15), $p < 0.05$	Median (range): 2.6 vs. 1.85 vs. 2.8, $p < 0.05$	Median (range): 1.57 vs. 1.47 vs. 1.77, $p > 0.05$	NM	NM	2/30 (6.7) vs. 1/30 (3.3) vs. 1/30 (3.3), $p = 0.47$	1/30 (3.3) vs. 2/30 (6.6) vs. 1/30 (3.3), $p = 0.347$	NM	Median (range): 6 vs. 6.6 vs. 7, $p = 0.17$
Piric, 2015, Bosnia and Herzegovina [26]	NM	NM	NM	Mean (SD): 80.9 (6.9) vs. 96.2 (4.4), $p < 0.05$	13/28 (46.4) vs. 12/30 (40), $p > 0.05$	1/28 (3.6) vs. 0/30, $p > 0.05$	4/28 (14.3) vs. 14/30 (46.6)	1/28 (3.6) vs. 1/30 (3.3)	Mean (SD): 8.6 (0.6) vs. 16.2 (1), $p < 0.01$
Müller, 2012, Switzerland [5]	Mean (SD): 60.4 (21.3) vs. 74 (21.6), $p = 0.006$	Mean (SD): 49.2 (21.3) vs. 55.8 (30), $p = 0.28$	Mean (SD): 40.6 (16.1) vs. 46.4 (20.1), $p = 0.21$	NM	13/40 (33) vs. 21/39 (54), $p = 0.06$	6/40 (15) vs. 10/39 (26), $p = 0.24$	8/40 (20) vs. 10/39 (26), $p = 0.55$	1/40 (3) vs. 4/39 (10), $p = 0.16$	Mean (SD): 10.8 (4.4) vs. 11.3 (4.5), $p = 0.49$

NM, not mentioned; N, number; h, hours.

the compared groups was statistically significant with a *p* value of <0.001, in favour of the coffee group (10.02 h, 95% CI 4.50–15.54; Fig. 3).

Time of First Defecation

Two studies provided data regarding the time of first defecation [25, 26]. A statistically significant difference ($p < 0.001$) was observed between the compared groups, in favour of the coffee group (16.14 h, 95% CI 13.70–18.59; Fig. 3).

Length of Hospital Stay

Three studies were included in the analysis regarding the duration of hospital stay [5, 25, 26]. No statistically significant difference was observed between compared groups (3.18 days, 95% CI 1.89–8.25; Fig. 3).

Discussion

Postoperative ileus constitutes a significant complication and optimal management is yet to be developed. Regarding the causative mechanism behind postoperative ileus, it has been proposed that a multitude of aetiologies may come into play such as the surgical manipulation itself, opioid analgesics, inflammation and imbalances in the autonomic function and gastrointestinal hormonal system [25]. Even though postoperative ileus is usually self resolving, it is a clinically and economically important consequence of major abdominal surgery. The pathophysiology concerning postoperative ileus is poorly defined and dependent on a multitude of factors; the most important of which are inflammation, the effects of surgical manipulation, administration of opioids, autonomic dysfunction, and deregulation of the gastrointestinal hormone activity and electrolyte fluctuations [27]. Unfortunately, therapeutic options for the prevention of ileus remain limited.

The role of enhanced recovery protocols is significant in the management of postoperative ileus. According to Sarawate et al. [28], hospital discharge was delayed, on average, by 3 days in patients that had postoperative ileus, when compared to patients who did not. This resulted in an increase of USD 4,000–9,000 in hospital expenses per patient undergoing abdominal surgery [28]. In light of the above, surgeons have attempted to combat this issue with a number of preventive measures [10]. These measures include early mobilization, laparoscopy instead of open surgery in order to keep surgical trauma to a minimum, the early rein-

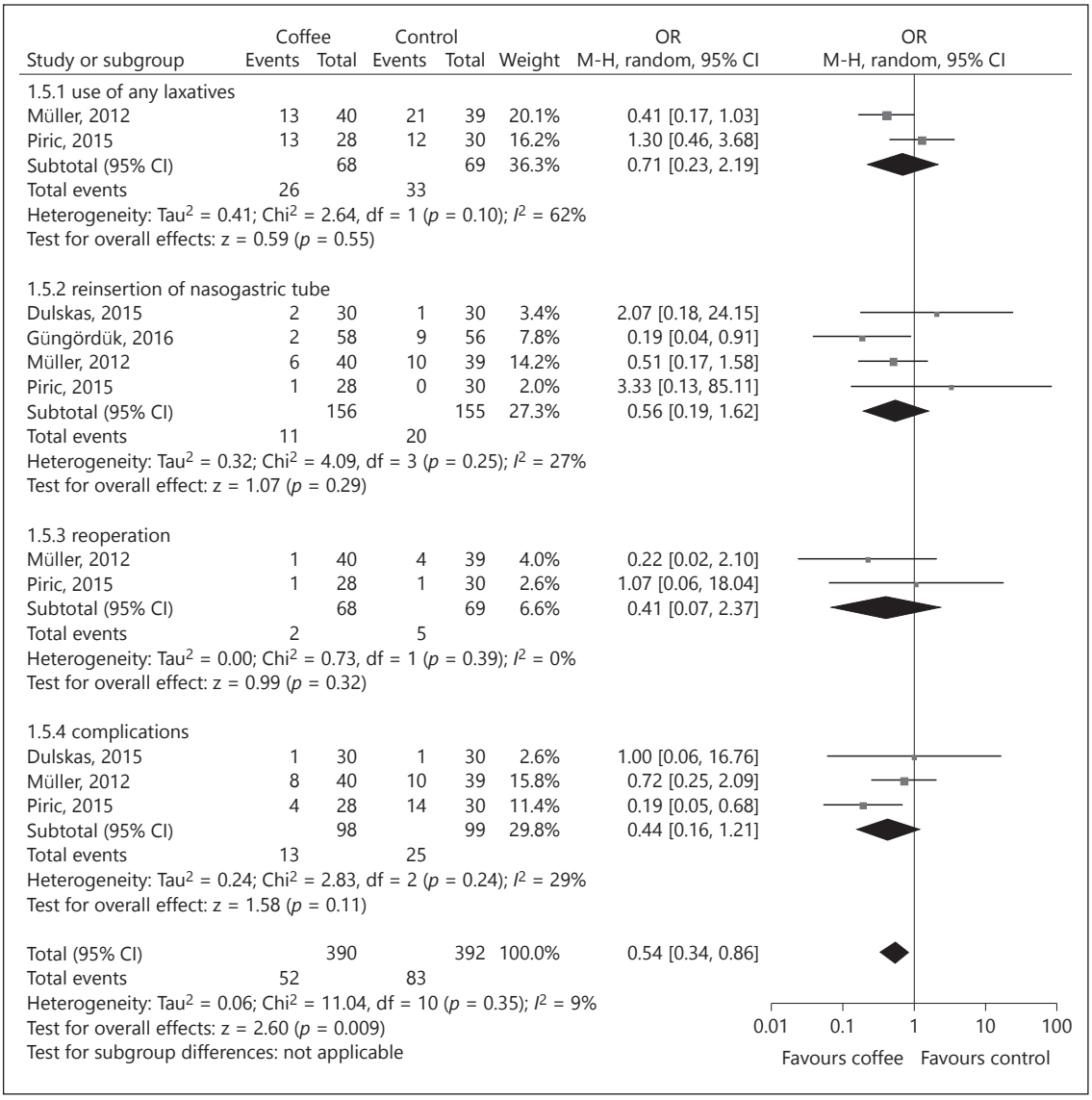

Fig. 2. Pooled ORs for the assessment of dichotomous data in the use of postoperative laxatives, the reinsertion of nasogastric tube, the need of reoperation and in complications (intraoperative and postoperative) in the coffee group(s) compared with the control group(s).

troduction of solid food in the patient's diet, the reduction in use of nasogastric tubes, thoracic epidural analgesia as well as the restriction of fluids [29]. The previously mentioned measures focus on optimizing analgesia and reducing stress and complications, with the ultimate goal of minimizing morbidity and enhancing recovery [30]. Enhanced recovery protocols can also include the administration of prokinetic agents (alvimopam, ghrelin agonists, neostigmine and serotonin receptor antagonists), chewing gum, gastrografin and coffee [5, 31–37].

Despite the extensive investigation in the physiological impact of coffee, information on how it impacts the bowel is scarce. Coffee has been shown to enhance colonic motility, within 4 min after consumption [25]. Caffeine is known to antagonize adenosine receptors, thus reducing motility. This can lead to the assumption that other biochemical agents may be those that exert the stimulatory effect. Dulskas et al. [24] reported a reduction in time to initiation of bowel movement with the administration of coffee without caffeine, when compared to the administration of regular coffee. This fact

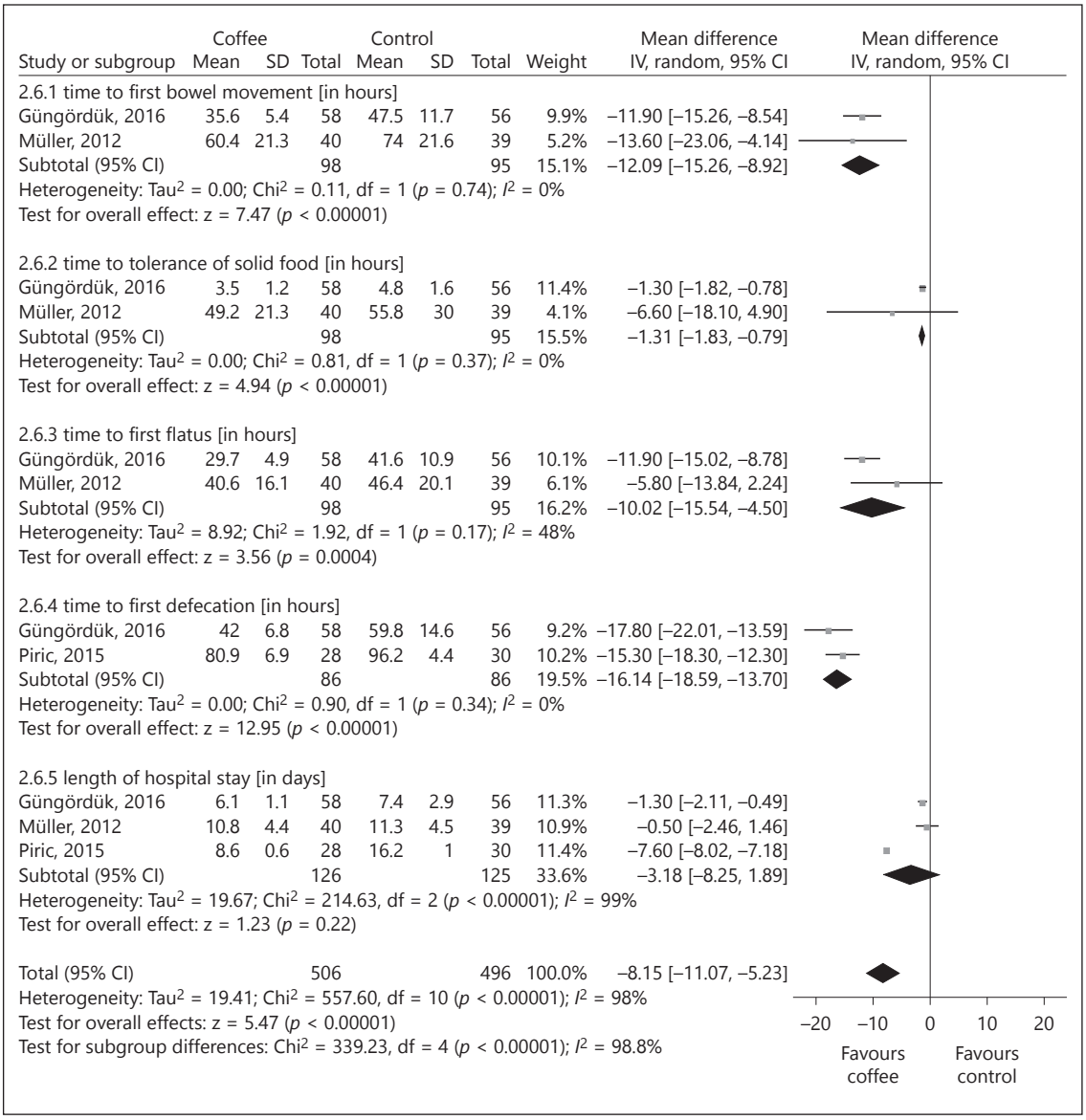

Fig. 3. Mean difference for continues data in time to first bowel movement (in hours), time to tolerance of solid food (in hours), time to first flatus (in hours), time of first defecation (in hours) and length of hospital stay (in days) in the coffee group(s) compared with the control group(s).

could be due to the formation of new active components during decaffeination. However, the biological mechanisms responsible for the stimulation of intestinal motility by coffee are still not well defined. Nonetheless, it could be hypothesized that coffee promotes intestinal motility while at the same preventing abdominal distension, abdominal pain and patient discomfort, which are all causative factors of postoperative ileus. In addition, the combination of good analgesia and coffee-induced intestinal motility facilitates the patient mobilization, minimizing the probability of postoperative intestinal paralysis and assisting the enhanced recovery of the surgical patient.

Several studies examined bowel movement, influenced by coffee consumption, hourly [5]. Coffee was found to be successful in activating bowel motility, but given that the advantage of a first bowel movement within the first 12 h post operation is not proven, Dulskas et al. [24] suggested that an improved result would be an earlier bowel movement by 24 h.

The gastrointestinal system can be stimulated by a meal due to its volume, caloric value, osmolality and acidity. Coffee, being of a pH of 5 (an acidity higher than that of beverages that do not enhance the gastrointestinal activity), and being in itself a low caloric drink, with an osmolality close to that of water, must exert its effect through the biochemical effect of other agents [24]. Some of the proposed culprits are chlorogenic acids or melonoidins [38, 39]. It has been found that up to 2 g/day of melanoidins may have an impact on the colon. Taking into account the recommended daily intake of fibre (10 g), melanoidins could be considered an important player in maintaining good health [38]. Information on the effect of chlorogenic acids is sparse. Another theory to elucidate the effect of decaffeinated coffee could be the formation of chemically active agents during decaffeinization.

Brown et al. [40] conducted a study in which motor rectosigmoidal function was monitored by way of multiport manometry in healthy subjects that indicated their inclination to defaecate after drinking coffee. The group that responded showed enhanced motility 4 min after drinking both regular and decaffeinated coffee, which was not the case in the group that did not respond. This response was not recorded after the ingestion of water. Rao et al. [21] studied the response in colonic motile activity to 240 mL regular coffee, decaffeinated coffee, water and a 1,000 Kcal meal, through ambulatory manometry via a catheter extending from the rectum to the mid-transverse colon. Increased motility and contractions were reported with the administration of regular coffee, coffee without caffeine and with feeding, when compared to water. Caffeinated coffee and a high-calorie meal induced a similar effect according to the study [21].

Piric et al. [26] conducted a study comparing CRP (C-Reactive Protein) levels (as a marker of postoperative complications), length of hospital stay, time to first bowel movement and rate of postoperative complications, among other parameters, between a group that was given tea and a group that was given coffee after the removal of the nasogastric tube on the first postoperative day. Subjects of the study were randomized, regarding the procedure performed, pathology (benign or malignant) and use of coffee. CRP levels were found to be significantly lower in the group that consumed coffee. In addition, CRP and time to initiation of bowel movements showed a positive correlation in both groups. Rates of complications after surgery were found to be decreased in the coffee group. Hospitalization time and time to initiation of bowel movements were also found to be reduced in the same group. These results were statistically significant. The authors disclosed that rates of right colon tumour and stapler anastomosis were not even between the 2 groups. Subsequently they analyzed the above parameters while controlling for diagnosis and anastomosis and concluded that in patients with a right colon tumour, those that were assigned to the coffee groups had lower CRP levels and a shorter hospital stay.

One of the aims of this study was to clarify if there is adequate evidence to support the use of coffee as a means of preventing ileus in the postoperative period. The present study showed that the postoperative administration of coffee reduces time to first bowel movement (a statistically significant result $p < 0.001$). In addition, both time to tolerance of solid food and time to first flatus were statistically significant in favour of the coffee group. Importantly, time to defecation was also statistically significant for the coffee group ($p < 0.001$). Safe conclusions could not be drawn regarding the additional use of laxatives, the necessity for the reinsertion of nasogastric tube or the need of reoperation as all the aforementioned outcomes did not presented any statistically significance. Regarding complications, they were not attributed to the administration of coffee. Furthermore, safe conclusions could not be reached regarding the length of hospital stay, which was not statistically significant, with a mean difference of 3.18 days per patient (95% CIs 1.89–8.25), and with high heterogeneity $I^2 = 99\%$. In accordance with other studies, no adverse effects were observed due to the consumption of coffee [5, 24–26].

The use of μ-receptor antagonists (such as alvimopan), in order to treat postoperative ileus caused by opioids, has also been studied [41]. Bell et al. [42] showed a correlation of alvimopan to a reduction in mean time to gastrointestinal recovery and a shorter by a single day hospitalization when compared to the control group. This resulted in a reduction of USD 900 per hospital stay. However, the average cost of coffee (5 cups to first bowel movement, USD 2.8 per patient), in comparison to the mean cost of treatment with alvimopan, indicates that coffee is a cheaper therapeutic strategy that offers comparable results [42].

A number of limitations should be taken into consideration in the interpretation of the findings of our analysis. The main disadvantage of the included studies was the heterogeneity of the patient population. Also, the age of patients, the different types of operations as well as the variation in both the quality and the quantity of administered coffee were the principal factors that increased the heterogeneity in this study. In addition, the existing studies have examined the role of coffee mainly on colorectal operations while there is no data regarding other surgical fields, such as urology, upper gastrointestinal surgery and

so on. In the present literature, there is also absence of studies which compare the administration of coffee during the postoperative period both in open and laparoscopic operations. Moreover, our literature search while extensive did not cover conference publications letters to the editor and animal studies. Lastly, language restriction was an extra limitation in our literature search.

Based on the limitations above, some points of criticism could be raised. Our review analyzes the additional value of coffee in the mobility of the bowel after surgery. Four studies met the inclusion criteria of the meta-analysis. Non randomized trials were excluded from the study. We concluded that the postoperative administration of coffee improves bowel motility reducing the time to first bowel movement, the time to first flatus and to defecation. The results could be interpreted with optimism; however, only 4 studies were analyzed and the postoperative setting of the studies was not very clear. For this reason, although our study showed good results, the use of coffee needs to be put in a wider postoperative setting. The enhanced recovery after surgery or fast track protocols further points that a patient should be followed up to improve the postoperative course. If our results are to be confirmed by more studies, coffee could be an integral part of the enhanced recovery after surgery clinical pathway.

Conclusion

In conclusion, the use of coffee as a means of postoperative ileus prevention can change the way to enhance recovery after surgery is applied. Even though, the mechanism of coffee's effect is not fully known, the currently available literature demonstrates a significant improvement in gastrointestinal motility and at the same time without having any impact on postoperative morbidity. Nevertheless, final conclusions could not be reached without the existence of studies with higher methodological quality and numbers that can offer a more careful evaluation of the clinical use of this popular beverage.

Disclosure Statement

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References

1 Asgeirsson T, El-Badawi KI, Mahmood A, Barletta J, Luchtefeld M, Senagore AJ: Postoperative ileus: it costs more than you expect. J Am Coll Surg 2010;210:228–231.
2 Lubawski J, Saclarides T: Postoperative ileus: strategies for reduction. Ther Clin Risk Manag 2008;4:913–917.
3 Vather R, Trivedi S, Bissett I: Defining postoperative ileus: results of a systematic review and global survey. J Gastrointest Surg 2013; 17:962–972.
4 Venara A, Neunlist M, Slim K, et al: Postoperative ileus: pathophysiology, incidence, and prevention. J Visc Surg 2016;153:439–446.
5 Muller 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;99:1530–1538.
6 Iyer S, Saunders WB, Stemkowski S: Economic burden of postoperative ileus associated with colectomy in the United States. J Manag Care Pharm 2009;15:485–494.
7 Tevis SE, Carchman EH, Foley EF, Harms BA, Heise CP, Kennedy GD: Postoperative ileus–more than just prolonged length of stay? J Gastrointest Surg 2015;19:1684–1690.
8 Livingston EH, Passaro EP Jr: Postoperative ileus. Dig Dis Sci 1990;35:121–132.
9 Johnson MD, Walsh RM: Current therapies to shorten postoperative ileus. Cleve Clin J Med 2009;76:641–648.
10 Kehlet H, Wilmore DW: Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg 2008;248:189–198.
11 Bragg D, El-Sharkawy AM, Psaltis E, Maxwell-Armstrong CA, Lobo DN: Postoperative ileus: recent developments in pathophysiology and management. Clin Nutr 2015;34:367–376.
12 Debarros M, Steele SR: Perioperative protocols in colorectal surgery. Clin Colon Rectal Surg 2013;26:139–145.
13 Hijazi Y, Gondal U, Aziz O: A systematic review of prehabilitation programs in abdominal cancer surgery. Int J Surg 2017;39:156–162.
14 Iavazzo C, Gkegkes ID: Enhanced recovery programme in robotic hysterectomy. Br J Nurs 2015;24:S4–S8.
15 Loop T: Fast track in thoracic surgery and anaesthesia: update of concepts. Curr Opin Anaesthesiol 2016;29:20–25.
16 Pecorelli N, Nobile S, Partelli S, et al: Enhanced recovery pathways in pancreatic surgery: state of the art. World J Gastroenterol 2016;22:6456–6468.
17 Wainwright TW, Immins T, Middleton RG: Enhanced recovery after surgery (ERAS) and its applicability for major spine surgery. Best Pract Res Clin Anaesthesiol 2016;30:91–102.
18 Lane JD, Pieper CF, Phillips-Bute BG, Bryant JE, Kuhn CM: Caffeine affects cardiovascular and neuroendocrine activation at work and home. Psychosom Med 2002;64:595–603.
19 Robertson D, Frolich JC, Carr RK, et al: Effects of caffeine on plasma renin activity, catecholamines and blood pressure. N Engl J Med 1978;298:181–186.
20 Johnston KL, Clifford MN, Morgan LM: Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. Am J Clin Nutr 2003;78:728–733.
21 Rao SS, Welcher K, Zimmerman B, Stumbo P: Is coffee a colonic stimulant? Eur J Gastroenterol Hepatol 1998;10:113–118.
22 Jadad AR, Moore RA, Carroll D, et al: Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–12.
23 Moher D, Pham B, Jones A, et al: Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? Lancet 1998;352:609–613.

24 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;58:1064–1069.
25 Gungorduk K, Ozdemir IA, Gungorduk O, Gulseren V, Gokcu M, Sanci M: Effects of coffee consumption on gut recovery after surgery of gynecological cancer patients: a randomized controlled trial. Am J Obstet Gynecol 2017;216:145 e1–154 e7.
26 Piric M, Pasic F, Rifatbegovic Z, Konjic F: The effects of drinking coffee while recovering from colon and rectal resection surgery. Med Arch 2015;69:357–361.
27 Vather R, O'Grady G, Bissett IP, Dinning PG: Postoperative ileus: mechanisms and future directions for research. Clin Exp Pharmacol Physiol 2014;41:358–370.
28 Sarawate CA, Lin SJ, Walton SM, Crawford SY, Goldstein JL: Economic burden of postoperative ileus (POI) in abdominal surgical procedures. Gastroenterology 2003;124:A828.
29 Rahbari NN, Zimmermann JB, Schmidt T, Koch M, Weigand MA, Weitz J: Meta-analysis of standard, restrictive and supplemental fluid administration in colorectal surgery. Br J Surg 2009;96:331–341.
30 Kehlet H, Dahl JB: Anaesthesia, surgery, and challenges in postoperative recovery. Lancet 2003;362:1921–1928.
31 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;29:1527–1534.
32 Drake TM, Ward AE: Pharmacological management to prevent ileus in major abdominal surgery: a systematic review and meta-analysis. J Gastrointest Surg 2016;20:1253–1264.
33 Flores-Funes D, Campillo-Soto A, Pellicer-Franco E, Aguayo-Albasini JL: The use of coffee, chewing-gum and gastrograffin in the management of postoperative ileus: a review of current evidence. Cir Esp 2016;94:495–501.
34 Short V, Herbert G, Perry R, et al: Chewing gum for postoperative recovery of gastrointestinal function. Cochrane Database Syst Rev 2015:CD006506.
35 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.
36 Toyomasu Y, Mochiki E, Morita H, et al: Mosapride citrate improves postoperative ileus of patients with colectomy. J Gastrointest Surg 2011;15:1361–1367.
37 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;30:225–232.
38 Stacewicz-Sapuntzakis M, Bowen PE, Hussain EA, Damayanti-Wood BI, Farnsworth NR: Chemical composition and potential health effects of prunes: a functional food? Crit Rev Food Sci Nutr 2001;41:251–286.
39 Vitaglione P, Fogliano V, Pellegrini N: Coffee, colon function and colorectal cancer. Food Funct 2012;3:916–922.
40 Brown SR, Cann PA, Read NW: Effect of coffee on distal colon function. Gut 1990;31:450–453.
41 Buchler MW, Seiler CM, Monson JR, et al: Clinical trial: alvimopan for the management of post-operative ileus after abdominal surgery: results of an international randomized, double-blind, multicentre, placebo-controlled clinical study. Aliment Pharmacol Ther 2008;28:312–325.
42 Bell TJ, Poston SA, Kraft MD, Senagore AJ, Delaney CP, Techner L: Economic analysis of alvimopan in North American Phase III efficacy trials. Am J Health Syst Pharm 2009;66:1362–1368.