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# The effect of chewing gum on postoperative ileus after laparotomy for gastroduodenal perforations: a randomized controlled trial

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## Abstract

**Background** Prolonged postoperative ileus is linked to a higher risk of additional complications, longer hospital stays, and higher healthcare expenses. There are few randomized controlled trials on the impact of chewing gum on the duration of ileus in patients undergoing emergency surgery, notably those with peritonitis. Compelling evidence from studies on elective procedures demonstrates that chewing gum can lessen the duration of ileus. This trial aimed to examine the effect of chewing gum on the length of the postoperative ileus which develop after laparotomy for gastroduodenal perforations.

**Materials and methods** Multicentre randomized controlled trial. Fifty-two patients were randomly assigned to two treatment groups. Group A received routine care with chewing gum, while group B only received routine care. The primary outcome was the length of postoperative ileus, while the secondary outcomes were the length of hospital stay, in-hospital morbidity, and mortality. The continuous variables were compared using the nonparametric Wilcoxon Rank sum (Mann-Whitney U) test while the categorical outcomes were compared using the chi-squared test in SPSS version 26. The protocol was retrospectively registered with the WHO Pan African Clinical Trial Registry (Number: **PACTR202206468032528**) on the 1st of June 2022.

**Results** Of the 52 participants included in the analysis, the majority were males (80.8%) with a mean age of 34.23 (SD = 11.52) years. There was no statistically significant difference in the baseline characteristics of the study participants between the two groups ( $P > 0.05$  for all). The median duration of postoperative ileus was 21.5 h less in the chewing gum group (28.5 versus 50.0,  $P = 0.002$ ), while the length of hospital stay was 2.5 days less in the chewing gum group (5.4 versus 7.9,  $P = 0.007$ ). There was no significant difference noted in the occurrence of complications.

**Conclusion** Chewing gum that is readily available and reasonably priced may help shorten the duration of postoperative ileus, which has the extra benefit of enabling early discharge.

**Keywords** Chewing-gum, Postoperative ileus, Sham feeding, RCTs, Africa

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## Introduction

After surgery, post-operative ileus (POI) happens when gastrointestinal motility briefly pauses without a known mechanical cause [1]. Prolonged postoperative ileus (PPOI) refers to a type of POI that persists on the fourth postoperative day [2]. Prolonged postoperative ileus has been linked to increased morbidity, lengthy hospital stays, and high healthcare expenses [3]. A study that looked at how POI affected patients having colectomies revealed that the expense of prolonged POI was comparable to the expense of re-admission with another major complication [4].

Gum chewing is thought to increase bowel movement by stimulating the cephalic-vagal pathway, which in turn increases gut myoelectric activity [5]. There is also speculation that this vagal activation has anti-inflammatory properties [6]. The first study that assessed the effect of chewing gum on the duration of postoperative ileus was done in 2002 among colon cancer patients [7]. According to this study [7], the length of hospital stays, flatus, and stool passage times were all shortened. Numerous studies including patients undergoing laparoscopic, open, elective, emergency, colorectal, gynecological, and many more, have been conducted over time with diverse results [1, 8–10]. In relation to the down sides of chewing gum, it cannot be given to patients that are not fully awake [11]. Also a sugared type of chewing gum has been reported to increase risk of dental caries [12], though rinsing and brushing regularly have been reported to mitigate this side effect [12, 13]. Others concerns may include issues such as difficulty chewing and poor tolerance among some patients.

There is a lack of information regarding the therapy of prolonged postoperative ileus, and the majority of the investigated drugs have had subpar results [6], thus preventive management is presently given top priority [14]. Enhanced recovery after surgery (ERAS) techniques have been shown to shorten POI length in elective surgeries, however, there is insufficient information on these measures for emergency surgeries [15]. The ERAS components that have been suggested for lowering POI in emergency surgeries are based on low-risk patients [15, 16], however, the majority of patients in low-income countries arrive too late and have a significant risk of peritonitis and morbidity [17].

Additionally, given that up to 20% of patients cannot tolerate early oral feeding, some clinicians avoid initiating feeds out of concern for the potential repercussions [9], yet early oral feeding is one of the main components of ERAS. Chewing gum may be an option for those patients in whom early oral feeding may not be considered an option. Most institutions in nations with low resources still consider minimally invasive surgery to be a pipe dream, yet minimally invasive surgery is one other

main component of ERAS. However, in places where the minimally invasive surgery component of ERAS is not feasible, the cheap and readily available chewing gum may be an option.

Most research on chewing gum for POI was conducted on elective procedures, primarily colorectal. Patients with gut perforations or peritonitis were not included in the mixed studies that included emergency surgeries [5]. This study was required to determine whether chewing gum can shorten the amount of time that patients with peritonitis have postoperative ileus. This study's primary objective was to examine the length of time needed for post-operative ileus to resolve, and its secondary objective was to compare the length of hospital stays, in-hospital morbidity, and mortality in the gum-chewing group of patients versus controls. The study's null hypothesis was that chewing gum does not affect the length of POI.

## Materials and methods

This research was approved by the research and ethics committee of Kampala International University (Ref: KIU-2021-60) and has been reported in line with the CONSORT criteria [18]. The detailed methodology including sample size determination was published in the trial protocol [19], thus, only being summarised below.

### Study participants

The surgical departments of three tertiary hospitals in Uganda were involved in this multicenter prospective randomized controlled study with a parallel superiority design. All patients with confirmed peritonitis due to gastric or duodenal perforation, between the age of 18 and 65 were included. The upper age limit was used because increasing age increases the risk of PPOI [8] yet we wanted the groups to be comparable. Patients with documented allergies to the contents of chewing gum, those with uncontrolled diabetes mellitus disease at the time of surgery, patients who were unconscious or unable to chew gum after 24 h post-surgery and patients with traumatic perforations were excluded. We enrolled 52 participants. Permuted balanced block randomization was conducted by the study supervisor to generate a random sequence of numbers to represent the two groups in an equal allocation ratio of 1:1.

### Inhospital care and chewing gum administration

Patients admitted in emergency department (ED) with suspected gastric or duodenal perforation based on clinical and radiological assessment were evaluated for eligibility and considered as possible candidates for the study. Routine pre-operative management for GDP was done for all patients as detailed in the published protocol [19]. All patients underwent omentoplasty. Post operatively patients in both groups received all the routine

post-operative care as detailed in the published protocol [19]. In addition to the routine post-operative care, patients in group A received chewing gum. Oral warm water was started on the first POD and if well tolerated, the volume was increased gradually, other liquids introduced and then solids later on.

Green PK brand chewing gum was used in this study. The patients in Group A were given green flavored PK and started chewing after regaining consciousness. The patients chewed 2 pellets of PK till they were tasteless three times in a day (morning, afternoon, and evening). The patients stopped chewing gum when POI resolved. Participants were instructed to inform the investigators if they experienced any challenges with chewing the gum. However, we did not have any such cases. Resolution of POI was defined as passage of stool or flatus or both in addition to fulfilling the criteria defined in the 6 domains described by the Tripartite gastrointestinal recovery post-operative ileus group such as absence of nausea and vomiting, having no need of nasogastric intubation, absence of abdominal pain and distension, and ability to tolerate oral feeds [20].

Patients were discharged if they passed stool and were tolerating oral feeds in the absence of any complication mandating continued admission irrespective of the post-operative day. If a patient was discharged before the 5th post operative day, intravenous antibiotics were stopped and oral antibiotics initiated to finish the 5-day course.

### Study variables

Primary outcome variable was time taken from end of surgery to resolution of ileus. Secondary outcome variables were duration of hospital stay in days (counted from time of admission to time of discharge), in-hospital morbidity and mortality. Morbidity was defined as any deviation from the postoperative course that was not inherent in the procedure and did not comprise a failure of cure and was reported in accordance with the Clavien Dindo classification 2004 [21]. The outcome assessors (attending physicians) were blinded about the ongoing study since chewing gum is not known to cause adverse effects that would warrant un-blinding. The recruiting team was totally different from the outcome assessors.

### Data analysis

The intention to treat model was used during analysis to minimize bias. Summarized data was analyzed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, USA, version 22.0 for Windows). To compare the time taken for post-operative ileus to resolve and length of hospital stay, the Shapiro-Wilks test revealed that the data was not normally distributed, therefore, the non-parametric Wilcoxon Rank sum (Mann-Whitney U) test was used. The receiver operator characteristic curve

(ROC) was used to further assess the association between chewing gum and POI as well as length of hospital stay. To compare the in-hospital morbidity and mortality, the chi squared test was used. All analyses were performed at 95% confidence level and a  $p$  value  $\leq 0.05$  was considered significant.

### Results

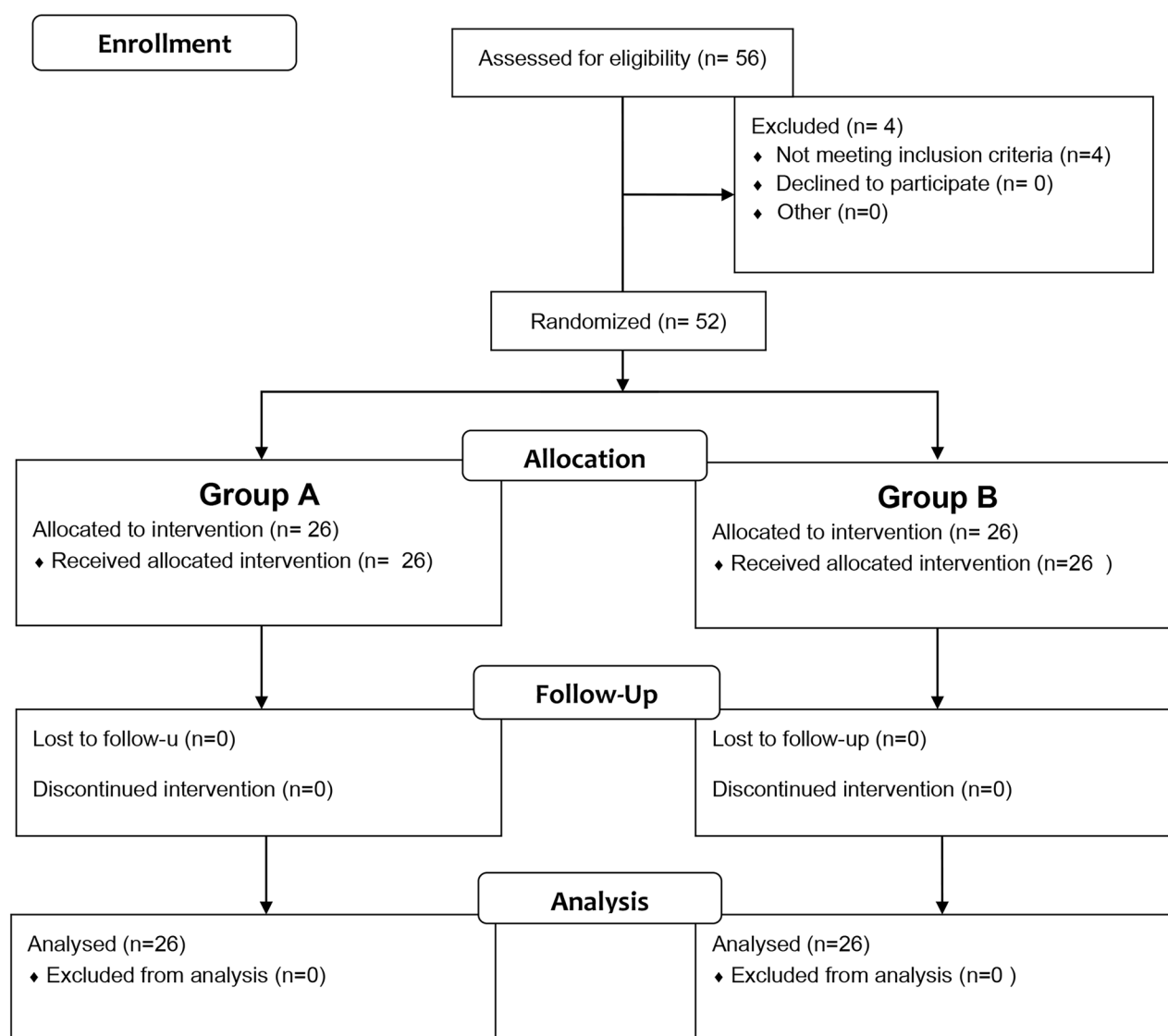
Over a period of four months starting on the 1st of April 2022, fifty-six patients were assessed for eligibility. Four were excluded because they had traumatic perforations. Of the remaining 52, 26 were allocated to group A (routine care plus chewing gum) and the other 26 to group B (routine care only). None was lost to follow up and all 52 were included in the final analysis (Fig. 1).

Of the 52 participants included in the analysis, the majority were males (80.8%) with a mean age of 34.23 (SD=11.52) years. The mean duration of symptoms at presentation was 4.69 (SD=3.35) days. The commonest perforation site was the pylorus (69.2%). There was no statistically significant difference in the baseline characteristics of the study participants between the two groups since all the  $P$  values were more than 0.05 (Table 1).

The median duration of postoperative ileus was 21.5 h less in the chewing gum group (28.5 versus 50.0,  $P=0.002$ ). Using the receiver operator characteristic curve (ROC), the area under the curve (AUC) was 0.749,  $P=0.002$  (Fig. 2). The median length of hospital stay was 2.5 days less in the chewing gum group (5.4 versus 7.9,  $P=0.007$ ). Using the ROC, the AUC was 0.716,  $P=0.008$  (Fig. 3). There was no significant difference noted in the occurrence of complications or the complications that occurred (Table 2). No deaths occurred among the 52 participants.

### Discussion

The primary objective of this study was to compare the time taken for post-operative ileus to resolve in the intervention group versus the controls and indeed we noted that patients who chewed gum had a significantly shorter duration of post-operative ileus. Our findings suggest that even in patients with peritonitis, administration of chewing gum postoperatively could be helpful in stimulation of bowel motility to result in early resolution of ileus. To the knowledge of the authors, this is the first study that has assessed the effect of chewing gum on the ileus in patients with gastroduodenal perforations, but some studies have been done evaluating the effect of chewing gum on the ileus in other emergency operations [5]: [22]. Our findings are in agreement with the results of Mahmoud et al. [5] who evaluated the effect of chewing gum in patients with acute appendicitis, and in line with the findings of Pilevarzadeh et al. [22] who evaluated chewing gum effect among patients who had cholecystectomy.



**Fig. 1** Consort flow diagram

In both studies, there was a significant reduction in the duration of ileus among patients who chewed gum even though the patients in these studies had localized peritonitis. In the rest of the related studies reviewed, the participants did not have peritonitis [23–26].

The secondary objective of this study was to compare the duration of hospital stay, in-hospital morbidity, and mortality in the intervention group versus the controls. Even though the patients who chewed gum had a significantly shorter length of hospital stay, there was no statistically significant difference noted in terms of post-operative complications between the two groups. This is in agreement with the findings reported by Ngowe et al. [27] who evaluated the effect of chewing gum in patients with acute appendicitis and reported that chewing gum

reduced the length of hospital by an average of 2 days. Other related studies reviewed did not report on length of hospital stay and those that reported were either mixed (emergency and elective) or elective alone [25, 26, 28, 29]. Though the early resolution of ileus noted in this study could have contributed to the reduced length of hospital stay, a keen look at the post-operative complications revealed that patients who did not chew gum had more complications that required a secondary procedure compared to those who did not chew gum. This difference in complications, though found not to be statistically significant, could have contributed to the increased length of hospital stay in the control group.

When examining the impact of chewing gum on the ileus, previous researchers have not focused on acute

**Table 1** Comparison of the baseline characteristics of the study participants between the two groups

Characteristic	Overall, N = 52	Chewing gum, N = 26	No chewing Gum, N = 26	P value
Categorical variables	n(% of 52)	n(% of 26)	n(% of 26)	
<b>Sex</b>				0.726 <sup>a</sup>
Male	42(80.8)	22 (84.6)	20 (76.9)	
Female	10(19.2)	4 (15.4)	6 (23.1)	
<b>History of Smoking</b>				0.324 <sup>a</sup>
Yes	12(23.1)	4 (15.4)	8 (30.8)	
No	40(76.9)	22 (84.6)	18 (69.2)	
<b>History of alcohol Intake</b>				1.000 <sup>a</sup>
Yes	17(32.7)	9 (34.6)	8 (30.8)	
No	35(67.3)	17 (65.4)	18 (69.2)	
<b>History of previous operation</b>				0.110 <sup>a</sup>
No	48(92.3)	26(100.0)	22 (84.6)	
Yes (Excision)	4(7.7)	0(0.0)	4 (15.4)	
<b>Urine output</b>				0.668 <sup>a</sup>
< 0.5 mls/hour	6(11.5)	4 (15.4)	2 (7.7)	
> 0.5 mls/ hour	46(88.5)	22 (84.6)	24 (92.3)	
<b>Perforation site</b>				0.295 <sup>a</sup>
Pyloric perforation	36(69.2)	16 (61.5)	20 (76.9)	
Lesser curvature site	8(15.4)	4 (15.4)	4 (15.4)	
Anterior body	8(15.4)	6 (23.1)	2 (7.7)	
<b>Electrolytes</b>				1.000 <sup>a</sup>
Deranged	4(7.7)	2 (7.7)	2 (7.7)	
Normal	48(92.3)	24 (92.3)	24 (92.3)	
<b>Hemoglobin</b>				1.000 <sup>a</sup>
Normal	48(92.3)	24 (92.3)	24 (92.3)	
Low	4(7.7)	2 (7.7)	2 (7.7)	
<b>Continues variables</b>	<b>Mean (SD)</b>	<b>Mean (SD)</b>	<b>Mean (SD)</b>	
Age in years	34.23(11.52)	33.77(13.54)	34.69(9.32)	0.776 <sup>b</sup>
Body mass index	24.47(3.21)	24.73(1.95)	24.21(4.13)	0.567 <sup>b</sup>
Duration of symptoms in days	4.69(3.35)	5.04(3.16)	4.35(3.56)	0.461 <sup>b</sup>
Size of perforation in cm	1.30(0.81)	1.50(0.89)	1.10(0.68)	0.076 <sup>b</sup>
Peritoneal fluid volume in liters	2.10(0.86)	2.32(0.83)	1.87(0.85)	0.056 <sup>b</sup>
Duration of operation in hours	1.63(0.44)	1.60(0.44)	1.65(0.45)	0.682 <sup>b</sup>

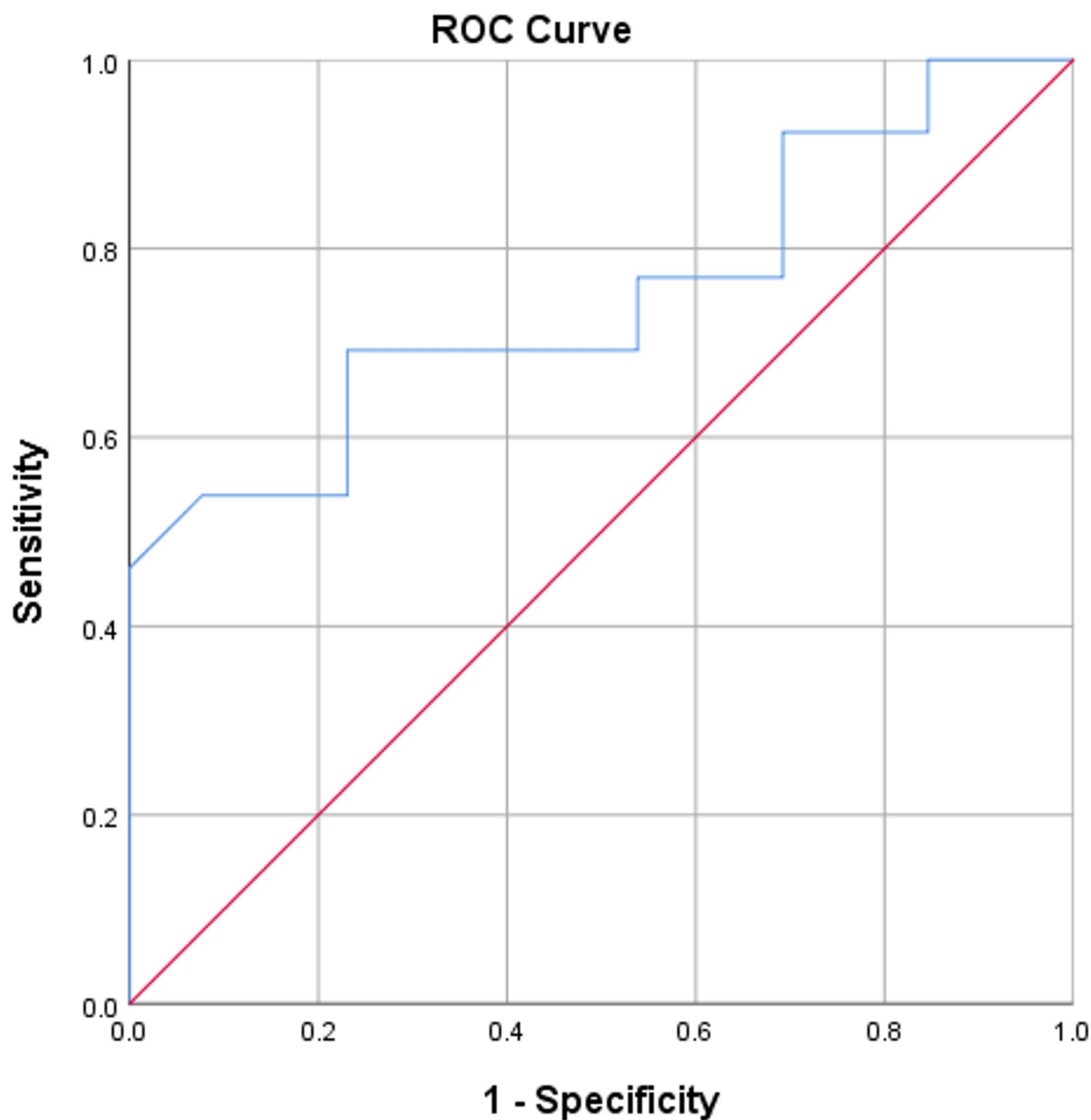
SD = standard deviation, a = Chi-squared p value, b = Independent samples T test p value.

peritonitis caused by gastroduodenal perforations. In the context of low-resource settings, which are frequently underrepresented in research papers, our study was timely in that it shed further light on the situation. Chewing gum that is readily available and reasonably priced may help shorten the duration of post-operative ileus, which has the extra benefit of enabling early discharge.

The pathophysiology of POI has been described as having two phases; the neural and inflammatory phases [26]. The neural phase occurs due to stimulation of mechanoreceptors and pain receptors at incising the skin but also, while manipulating the bowel [26]. This activation starts a neural reflex that depends on presence of substance P and  $\alpha$ -calcitonin, causing inhibition of bowel movement [26]. The inflammatory phase results from release of mediators of inflammation in the gut wall [26]. The handling of the bowel starts a cascade of inflammation that starts activating and degranulating mast cells [26]. These

activated mast cells in turn activate resident macrophages which release cytokines and chemokines hence attracting neutrophils to the gut wall [26]. This impairs the ability of the smooth muscle cells to contract by releasing nitric oxide and prostaglandins [26].

In some patients with peritonitis such as those with gastroduodenal perforations, ileus is already present even before surgery. Gastroduodenal perforations are commonly caused by peptic ulcer disease [17]. Following perforation there is leakage of stomach or duodenum contents causing a chemical peritonitis first, then sepsis [17]. Ileus is one of the main presenting symptoms of gastroduodenal perforations [17] which makes prolonged post operative ileus more likely in these patients. One study in Uganda reported that prolonged post operative ileus was among the top four complications following gastroduodenal perforation surgery [30].



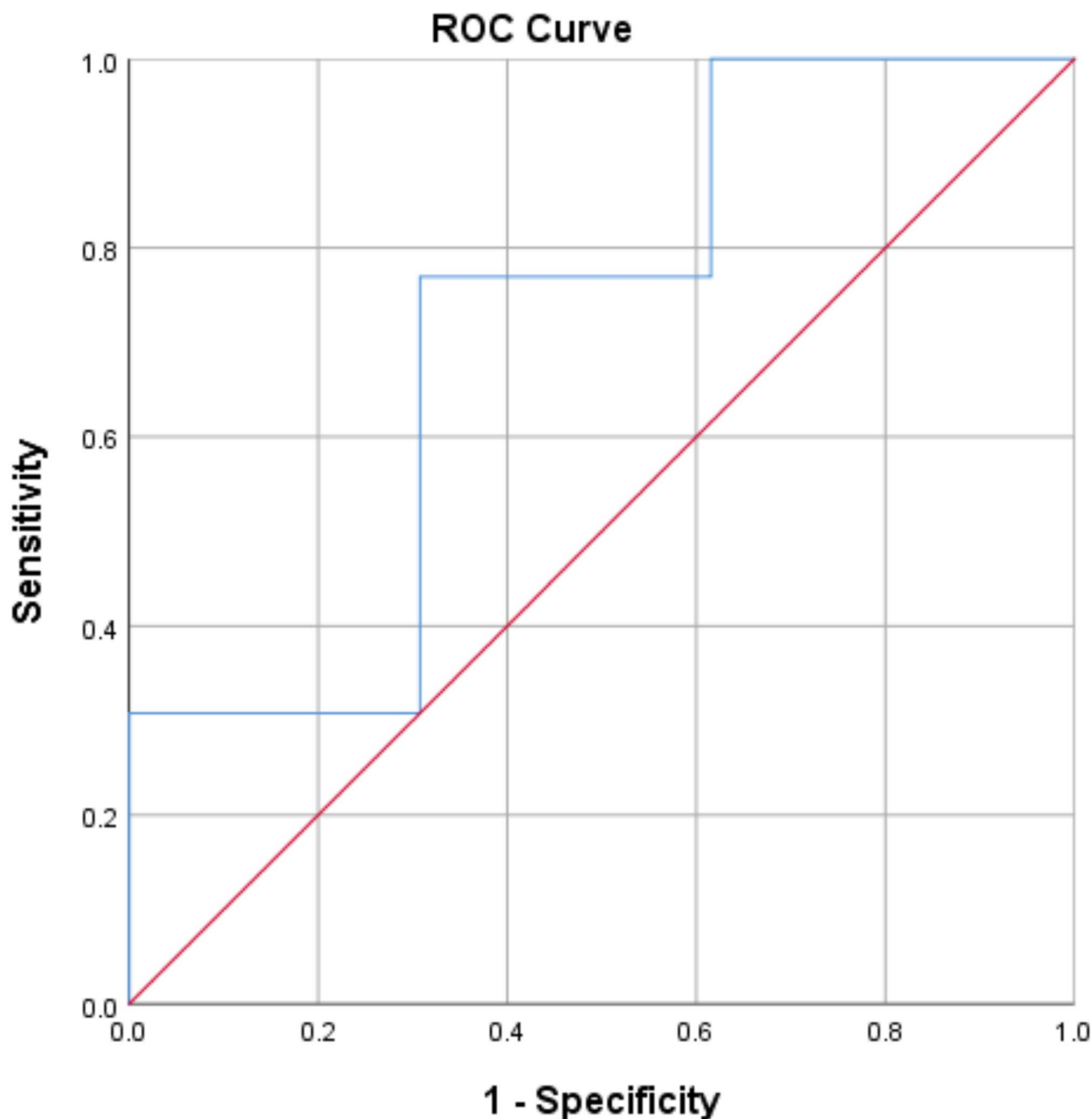
**Fig. 2** Receiver operator characteristic curve for duration of post operative ileus

The vagus nerve provides innervation to the gut and the stimulation of the vagus nerve branches in the cephalic phase, causes autonomic responses such as increased gastrointestinal motor activity and the release of gastrointestinal hormones and enzymes [31]. The cephalic phase begins when one thinks about a meal, and stops when one first swallows. Chewing causes salivation and stimulates sensory nerve endings in the mouth hence enhancing the vagal response [31]. Chewing gum resembles eating and is a form of sham feeding [32], which

increases the blood levels of gastrointestinal hormones [33]. Sham feeding is reported to improve gut motility by activating the cephalic-vagal pathway, resulting in stimulation of gut myoelectric activity and stimulating intestinal movement [5]. This vagal stimulation is also thought to have an anti-inflammatory effect [6].

#### Limitations

Our relatively small sample size and exclusion of individuals with concomitant conditions limit the



**Fig. 3** receiver operator characteristic curve for length of hospital stay

generalizability of the study findings, but we hope that the results will serve as a baseline for future, bigger multicenter randomized controlled studies. More so, since any placebo in this situation would also count as sham feeding, the subjects in this trial were unblinded early. The results are only partially generalizable in this situation since we only enrolled individuals with gastroduodenal peritonitis, which may not have a large bacterial burden compared to other gastrointestinal perforations.

Excluding patients with significant comorbidities such as uncontrolled diabetes reduces the study's generalizability.

### Conclusions

The results of this trial demonstrate that chewing gum is effective in reducing the duration of postoperative ileus and length of hospital stay among patients who present with peritonitis secondary to gastroduodenal perforations, justifying the potential for its consideration in the post-operative care of these patients. We recommend a



**Table 2** Comparison of the primary and secondary outcomes between the two groups

Outcome	Overall, N = 52	Chewing gum, N = 26	No chewing Gum, N = 26	P value
<b>Continuous variables</b>	<b>Median (IQR)</b>	<b>Median (IQR)</b>	<b>Median (IQR)</b>	
Duration of postoperative ileus (hours)	32.0(21.0–50.0)	28.5(15.0–36.1)	50.0(25.2–65.9)	<b>0.002<sup>c</sup></b>
Length of hospital stay (days)	7.6(3.9–16.3)	5.4(3.6–10.9)	7.9(6.8–24.6)	<b>0.007<sup>c</sup></b>
<b>Categorical variables</b>	<b>n(% of 52)</b>	<b>n (% of 26)</b>	<b>n (% of 26)</b>	
<b>Complications</b>				1.000 <sup>d</sup>
No	40(76.9)	20 (76.9)	20 (76.9)	
Yes	12(23.1)	6 (23.1)	6 (23.1)	
<b>Complication type</b>				0.083 <sup>d</sup>
None	40(76.9)	20 (76.9)	20 (76.9)	
Leakage	6(11.5)	2 (7.7)	4 (15.4)	
Burst abdomen	2(3.8)	0(0.0)	2 (7.7)	
SSI	4(7.7)	4 (15.4)	0(0.0)	

IQR = Interquartile range c = Mann-Whitney U test p value, d = Chi-squared p value

larger multi-center randomized controlled trial including patients with peritonitis arising from small and large bowel perforations to further examine the generalisability of our findings. This study was limited to patients undergoing laparotomy, therefore effect of CG among patients undergoing minimally invasive surgery (MIS) was not assessed. Since relatively more patients in non-chewing gum group had leakage and burst abdomen, these complications could have increased the duration of POI and LOS. However, it is difficult to ascertain if the chewing gum was responsible for the lower rate of these complications in the chewing gum group, given that the association between chewing gum and complications was not significant.

#### Abbreviations

ERAS Enhanced recovery after surgery  
POI Post-operative ileus  
PPOI Prolonged postoperative ileus

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#### Author contributions

JM was the principal investigator, conceived and designed the study, collected data, analysed the data, discussed the results, and wrote the draft of the manuscript. SFM, GNB, MAW, SMK, KMS, MML, BPK, ETT, TMF and HL revised the methodology, discussed the results, and revised the manuscript. HL additionally supervised the study and critically reviewed the manuscript. All authors approved the final manuscript submitted.

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#### Data availability

Data is available upon request. Requests should be sent to joshuablessed7@gmail.com (JM). The data collection materials are available as part of the protocol published in the International Journal of Surgery Protocols (reference 19 in the manuscript).

#### Declarations

##### Ethics approval and consent to participate

This study adhered to the Declaration of Helsinki. All methods were conducted in accordance with relevant guidelines and regulations. Ethical approval was granted by the Research and Ethics Committee of Kampala International University (Ref No: KIU-2021-60). All participants gave written informed consent as evidenced by the participants' signature.

##### Consent for publication

Not applicable.

##### Competing interests

The authors declare no competing interests.

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