Gastric Emptying Time of Oligomeric Formula in Adult Males

Original Article

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ABSTRACT

Background: We conducted two clinical studies on the gastric emptying time of oligomeric formula in men to help estimate safe preoperative fasting times in patients receiving enteral nutrition.

Methods: In Study 1, 10 adult male volunteers orally ingested fat-free oligomeric formula and a clear fluid on different days. The cross-sectional area (CSA) of the gastric antrum was measured by abdominal ultrasonography in the right lateral decubitus position every hour until the area was ≤4.0cm^2, or up to 4h after ingestion.

In Study 2, 6 adult male volunteers orally ingested fat-containing oligomeric formula, a clear fluid, and rice balls on different days. The CSA was measured every hour until the area was ≤4.0cm^2, or up to 6h after ingestion.

Results: In Study 1, gastric emptying time was longer for fat-free oligomeric formula (3.5 [3-4] h) than for clear fluid (1 [1-2] h) (p<0.0001). In Study 2, gastric emptying time was not statistical different between fat-containing oligomeric formula (4.5 [3-5] h) and rice balls (4 [4-4.25] h), and the times were longer for both of these than for clear fluid (1.5 [1-2] h) (p<0.0001). Gastric emptying time never exceeded 4h after ingestion of fat-free oligomeric formula or 5h after ingestion of fat-containing oligomeric formula or rice balls.

Conclusions: Gastric emptying time appears to be approximately 4h for fat-free oligomeric formula and about 5h for fat-containing oligomeric formula, which may be comparable to the time of rice balls.

Key Words: Gastric emptying time, Oligomeric formula, Ultrasound assessment.

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INTRODUCTION

Eating and drinking are restricted before elective surgery with general anesthesia due to the risk of vomiting and aspiration during induction of anesthesia. Longer preoperative fasting is safer, but causes patients distress from thirst and hunger[1]. Recent studies have demonstrated the safety and effectiveness of shorter fasting, and the Japanese Society of Anesthesiologists (JSA) has published preoperative fasting guidelines for clear fluids, breast milk, baby formula, and cow's milk to reduce preoperative fasting times safely. However, the guidelines do not provide any information on fasting times for enteral formula. Similarly, the guidelines of the American Society of Anesthesiologists (ASA) and the European Society of Anaesthesiology (ESA) do not mention fasting times for enteral formula[2,3].

Thus, there is currently no guidance on preoperative fasting time for elective surgery with general anesthesia in patients receiving enteral nutrition, and the appropriate fasting time for these patients remains unknown. We conducted clinical studies to investigate the gastric emptying time of oligomeric formula in men to help estimate safe preoperative fasting times in patients receiving enteral nutrition.

METHODS

Study 1: Fat-free oligomeric formula:

The study was approved by the Institutional Review Board of Yamaguchi University Hospital (No. H2020-099) and registered in the UMIN Clinical Trials Registry (UMIN 000041703). Written informed consent was obtained from all participants.

This was a crossover study with 10 adult male volunteers assigned to two groups with simple randomization methods using computer-generated number, Group A (n= 4) and Group B (n= 6) (Figure 1). Group A

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orally ingested fat-free oligomeric formula (two 200-ml bottles of Peptino®) first and then clear fluid (500-ml sports drink) on a later date. Group B orally ingested clear fluid first and then fat-free oligomeric formula on a later date. On the day of the study, participants stopped eating at midnight and stopped drinking any liquids at 6:00AM. At around 9:00AM, the cross-sectional area (CSA) of the gastric antrum was measured by abdominal ultrasonography in the right lateral decubitus position to confirm whether it was ≤4.0cm^2. To measure the CSA of the gastric antrum on ultrasonography, the area was taken to be an ellipse, the long axis and short axis were measured, and the area calculation was performed (long axis×short axis×π/4) (Figure 2). The participant orally ingested their assigned beverage within a 5-min period, and the CSA of the gastric antrum was measured again immediately after ingestion. The CSA of the gastric antrum was then measured every hour until it was ≤4.0cm^2, or up to 4h after ingestion. The time after ingestion until the CSA of the gastric antrum was confirmed to be ≤4.0cm^2 was defined as the gastric emptying time.

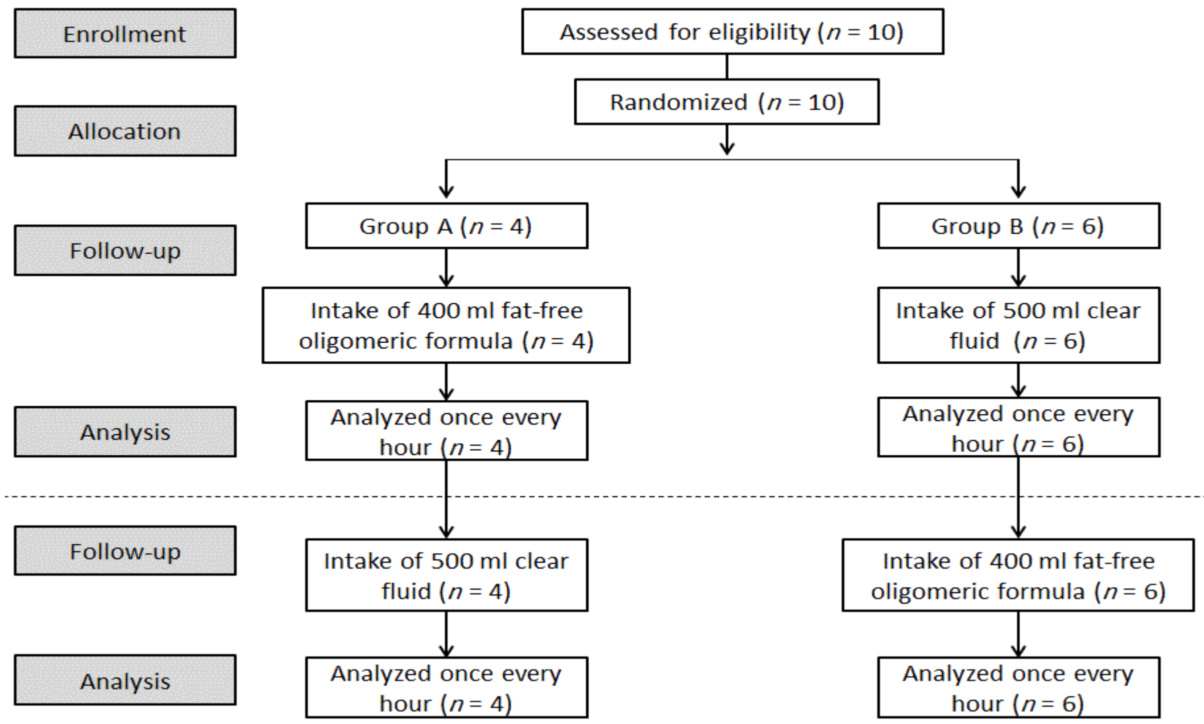

Fig. 1: Flow chart of Study 1.

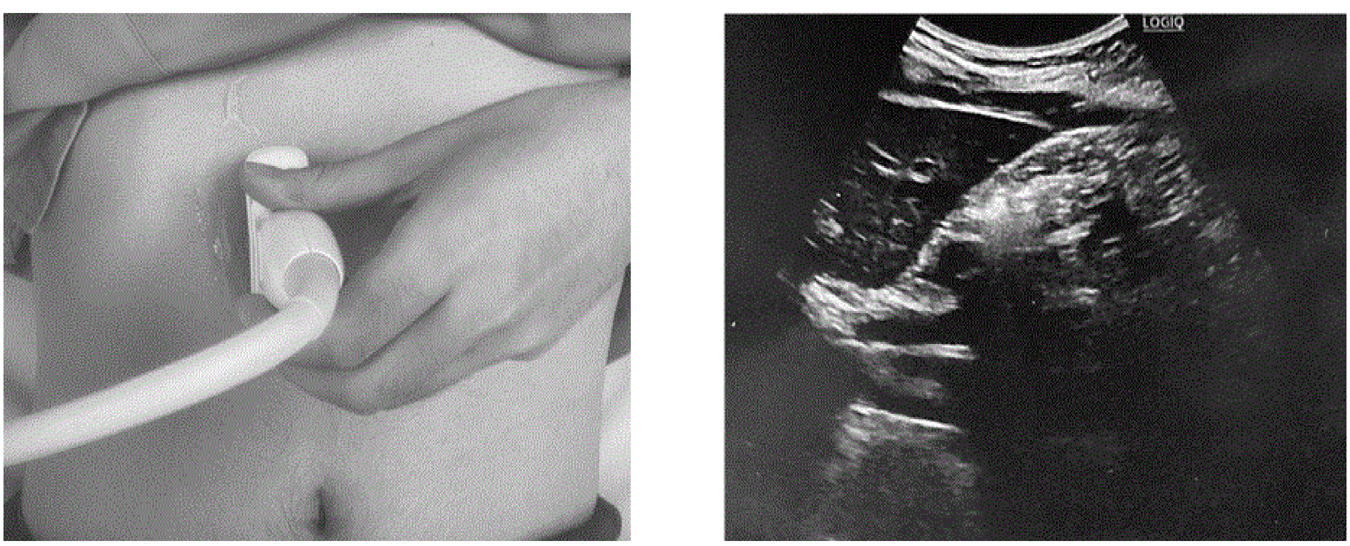

Fig. 2: Measurement of the cross-sectional area of the gastric antrum by ultrasonography. (A) The ultrasound probe was applied longitudinally to the midline of the upper abdomen, offset slightly to the right, with the patient in the right lateral decubitus position. (B) The cross-sectional area of the gastric antrum was depicted while aiming at the inferior vena cava or aorta and superior mesenteric artery (SMA).

Study 2: Fat-containing oligomeric formula:

The study was approved by the Institutional Review Board of Yamaguchi University Hospital (No. H2022-049-2) and registered in the UMIN Clinical Trials Registry (UMIN 000047461). Written informed consent was obtained from all participants.

This was a clinical study conducted with 6 adult male volunteers. Participants orally ingested fat-containing oligomeric formula (two 200-ml bottles of Peptamen Standard®), a clear fluid (400-ml sports drink), and rice balls (two commercially available 100-g plain salted rice balls). Since there was no significant difference between Group A and Group B in Study 1, the order of ingestion was not randomized in Study 2. The other methods are the same as those in Study 1, except that the measurement of CSA was continued up to 6h after ingestion.

Statistical Aanalysis:

Continuous variables are expressed as the median [interquartile range]. In Study 1, assuming the difference in gastric emptying time between oligomeric formula and sports drink of 1 hour and the standard deviation of 1 hour, the required number of enrollments would require 10 participants with α= 0.05 and 1-β= 0.8. Participant characteristics, gastric emptying time, and the CSA of the gastric antrum at each hour were compared between Group A and Group B using the Wilcoxon rank-sum test. The CSA of the gastric antrum at each hour and gastric emptying time were compared between the clear fluid and fat-free oligomeric formula groups using the Wilcoxon rank-sum test. In Study 2, assuming the difference in gastric emptying time between oligomeric formula and sports drink of 1 hour and the standard deviation of 0.63 hour from the result of Study 1, the required number of enrollments would require 6 participants with α= 0.05 and 1-β= 0.8. The CSA of the gastric antrum at each hour and gastric emptying time were compared between the clear fluid group, fat-containing oligomeric formula group, and rice ball group using the Kruskal–Wallis test and Mann–Whitney *U* test. The Bonferroni correction was used for the Mann–Whitney *U* test. Results with $p<0.05$ were considered statistically significant. All statistical analyses were performed using JMP® Pro 15.0.0 (SAS Institute Inc., Cary, NC).

RESULTS

Study 1: fat-free oligomeric formula:

Participants' age, height, and weight were 40 [32-51] years, 172.5 [169.0-176.8] cm, and 69.0 [58.3-76.5] kg in the group that received fat-free oligomeric formula first (Group A) and 33 [26-35] years, 170.5 [163.8-180.3] cm, and 66.8 [56.0-70.8] kg in the group that received clear fluid first (Group B). Participant characteristics were not significantly different between the groups.

Gastric emptying time was longer for fat-free oligomeric formula (3.5 [3-4] h) than for clear fluid (1 [1-2] h) ($p < 0.0001$). Moreover, gastric emptying time did not exceed 4 h in any participant (Figure 3).

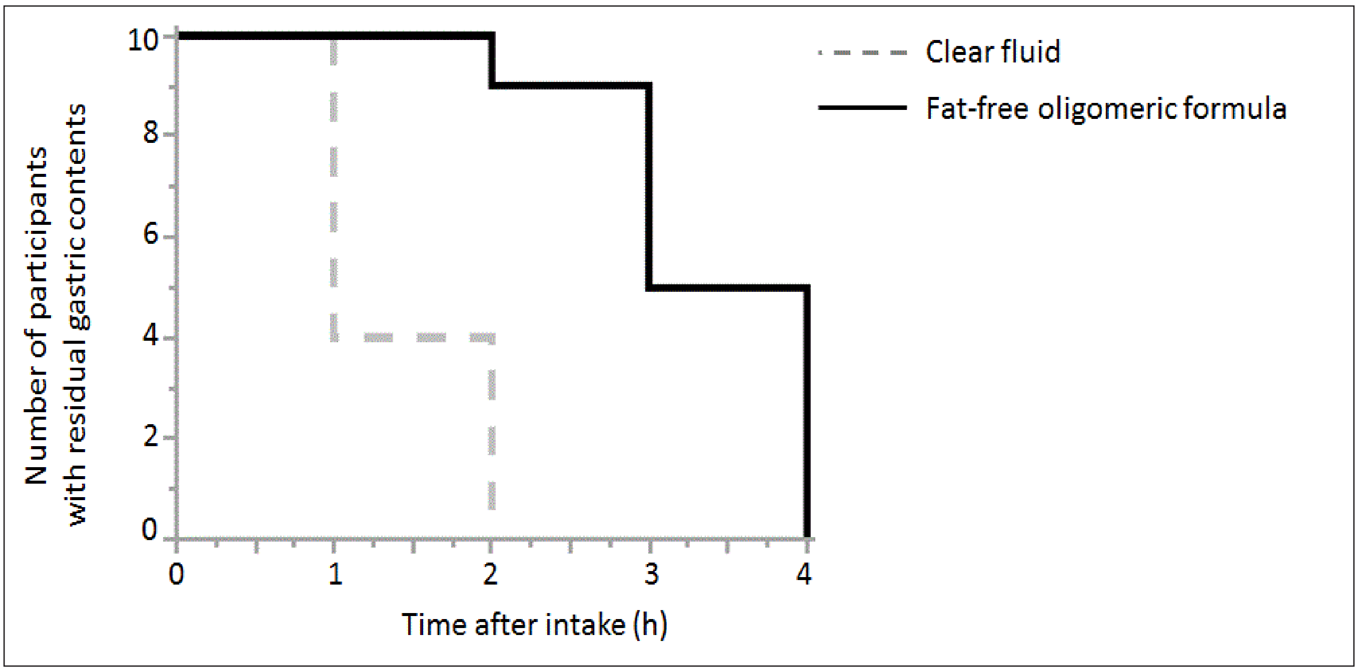

Fig. 3: Change in the number of participants with residual gastric contents in Study 1. The horizontal axis shows the elapsed time after oral intake, and the vertical axis shows the percentage of participants with residual gastric contents. Solid line, fat-free oligomeric formula. Dash line, clear fluid.

Neither gastric emptying time nor CSA of the gastric antrum differed significantly for clear fluid or fat-free oligomeric formula in Group A versus Group B (Table 1). The CSA of the gastric antrum immediately after ingestion was 14.1 [8.1-19.6] cm^2 for clear fluid and 13.7 [10.3-19.4] cm^2 for fat-free oligomeric formula, with no significant difference between them (p= 0.73). This area rapidly decreased at 1h after ingestion of clear fluid, but the decrease after ingestion of fat-free oligomeric formula was much more gradual, with the area at 1 h after ingestion differing little from the area immediately after ingestion (Figure 4).

Table 1: Comparison between Group A and Group B in Study 1:

	Group A (n= 4)	Group B (n= 6)	p value
Clear fluid			
Gastric emptying time (h)	1 [1-1.75]	1.5 [1-2]	0.49
CSA of the gastric antrum (cm^2)			
Before	3.1 [2.6-3.5]	1.6 [0.9-2.7]	0.06
After 0h	15.5 [9.8-22.8]	11.9 [6.2-17.7]	0.48
1h	3.4 [1.8-7.3]	4.2 [3.1-7.2]	0.61
2h	-	1.2 [1.1-3.6]	-
Fat-free oligomeric formula			
Gastric emptying time (h)	3.5 [3-4]	3.5 [2-4]	0.73
CSA of the gastric antrum (cm^2)			
Before	2.4 [1.6-3.1]	2.2 [2.1-3.1]	0.90
After 0h	11.0 [10.1-16.8]	15.5 [11.6-22.2]	0.27
1h	18.3 [10.0-24.1]	14.1 [10.3-16.3]	0.29
2h	9.4 [5.9-15.7]	10.1 [7.5-13.7]	0.95
3h	4.5 [3.0-10.2]	8.2 [2.4-11.3]	0.68
4h	3.8 [3.6-3.9]	3.9 [3.7-3.9]	0.92

Data are presented as the median [interquartile range]. CSA: Cross-sectional area.

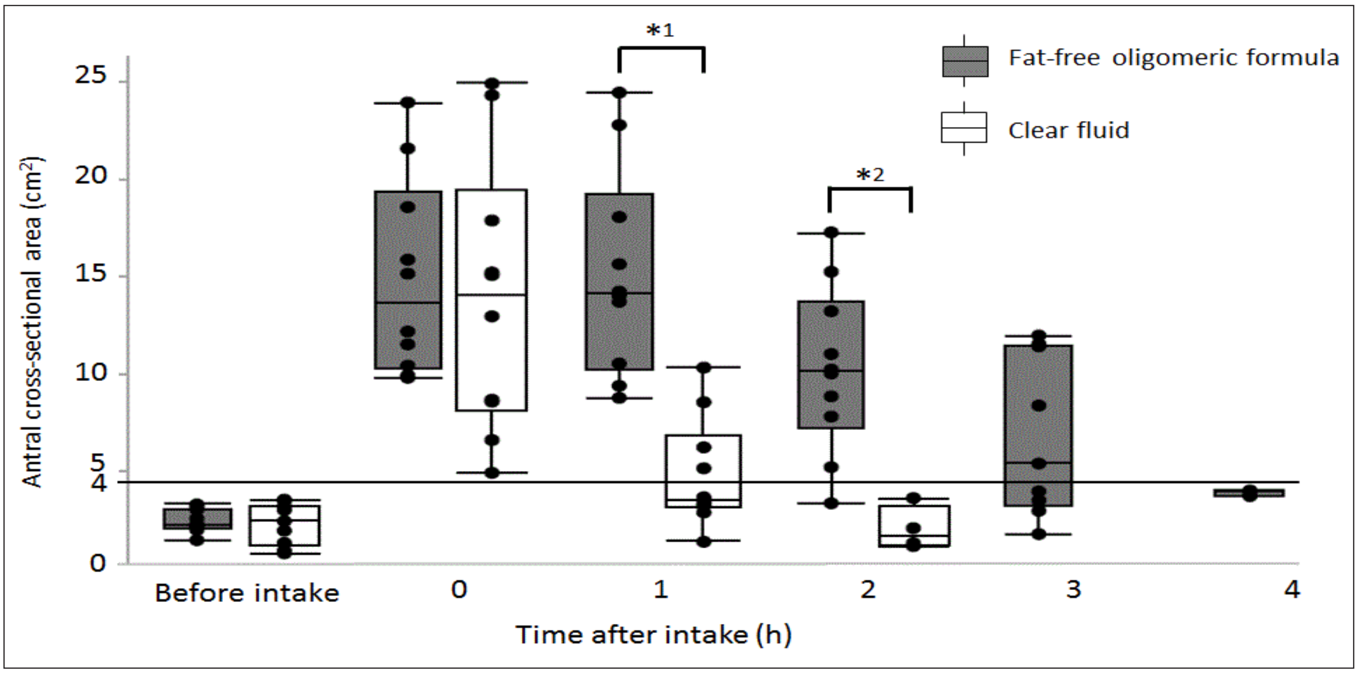

Fig. 4: Change in the cross-sectional area of the gastric antrum in Study 1. The horizontal axis shows the elapsed time, and the vertical axis shows the cross-sectional area of the gastric antrum. Left, fat-free oligomeric formula. Right, clear fluid. *: p<0.0001; **: p= 0.003.

Study 2: fat-containing oligomeric formula:

Participants' age, height, and weight were 33 [28-41] years, 173.5 [168.8-176.3] cm, and 64.5 [58.0-69.3] kg. Gastric emptying time was comparable between fat-containing oligomeric formula (4.5 [3-5] h) and rice balls (4 [4-4.25] h), and both of these times were longer than the gastric emptying time of clear fluid (1.5 [1-2] h) (p<0.0001). Moreover, gastric emptying time never exceeded 2 h after ingestion of clear fluid or 5h after ingestion of fat-containing oligomeric formula or rice balls (Figure 5).

The CSA of the gastric antrum immediately after ingestion was 16.4 [9.1-22.0] cm^2 for clear fluid, 14.3 [13.2-18.3] cm^2 for fat-free oligomeric formula, and 11.0 [5.8-14.5] cm^2 for rice balls, with no significant difference among them (p= 0.32). As in Study 1, the area decreased rapidly at 1h after ingestion of clear fluid. In contrast, the area after ingestion of fat-containing oligomeric formula or rice balls decreased little from immediately after ingestion even up to 2h after ingestion, and this decrease was significantly slower, with no difference between the oligomeric formula and rice balls (Figure 6).

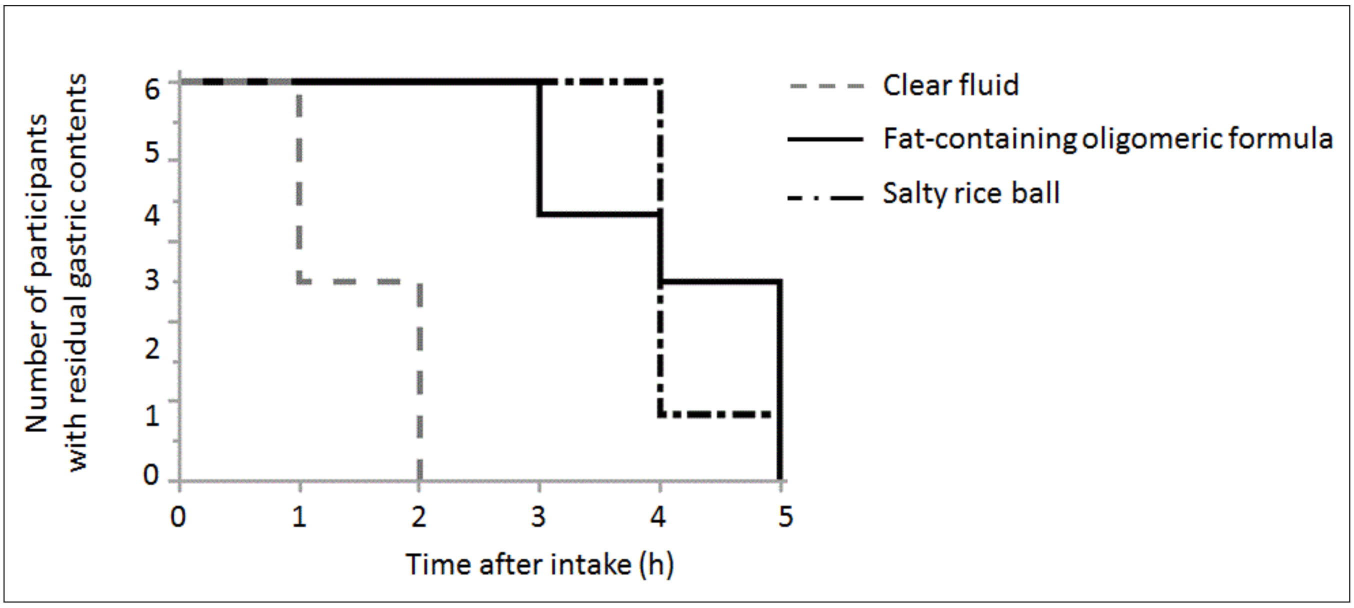

Fig. 5: Change in the number of participants with residual gastric contents in Study 2. The horizontal axis shows the elapsed time after oral intake, and the vertical axis shows the percentage of participants with residual gastric contents. Solid line, fat-containing oligomeric formula. Dashed line, clear fluid. Dash-dotted line, rice ball.

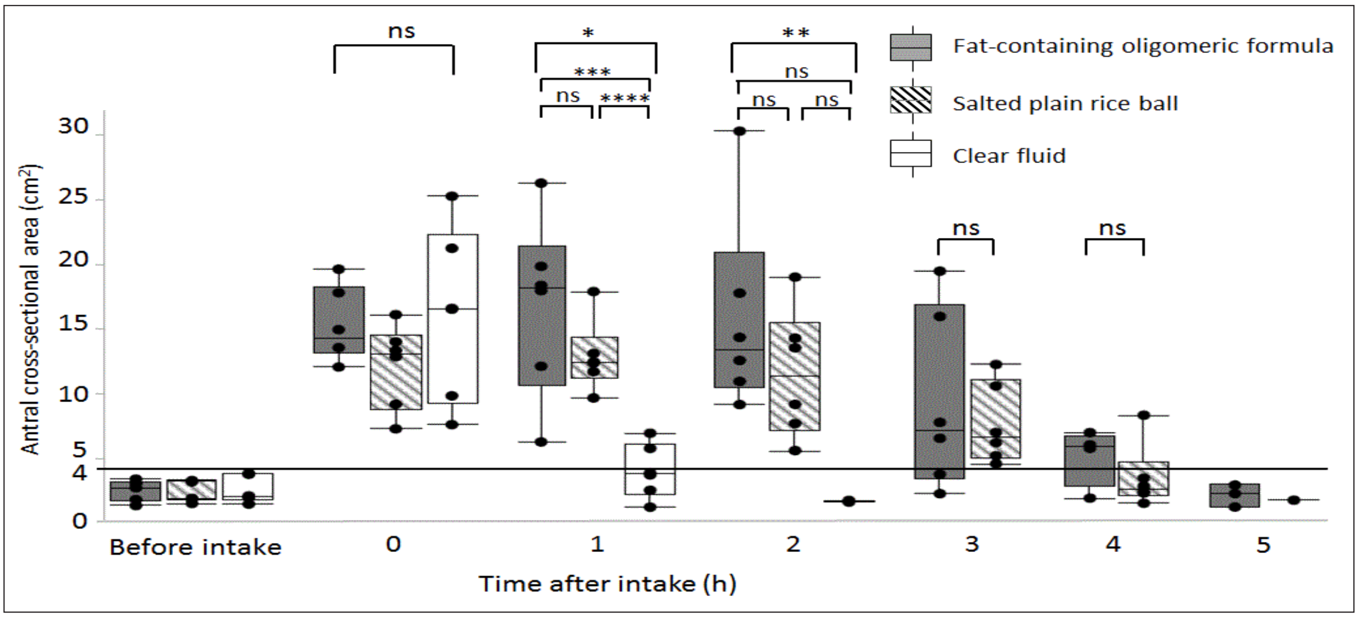

Fig. 6: Change in the cross-sectional area of the gastric antrum in Study 2. The horizontal axis shows the elapsed time, and the vertical axis shows the cross-sectional area of the gastric antrum. Left, fat-containing oligomeric formula. Center, rice balls. Right, clear fluid; *: p= 0.0005; **: p= 0.0493; ***: p= 0.0082; ****: p= 0.0051; ns: not significant.

DISCUSSION

In recent years, Enhanced Recovery after Surgery (ERAS) protocols, preoperative fasting guidelines, and oral rehydration therapy (ORT) have advocated shortening preoperative fasting times. Fearon *et al.,*[4] recommended stopping solid food 6h prior to surgery and water 2h prior to surgery as part of the ERAS protocol. Hausel *et al.,*[5] showed that ORT reduces preoperative thirst, hunger, and anxiety and significantly decreases postoperative insulin resistance.

Guidelines, including those of the JSA, ASA, and ESA, recommend stopping intake of clear fluids 2h before surgery[2, 3]. The preoperative fasting guidelines of the JSA do not specify a clear fasting time for solid food due to lack of evidence on solid food, the unclear definition of solid food, and the variability of nutrients in solid food. However, the ESA guidelines recommend a fasting time of 6h[3], and the ASA guidelines recommend abstaining from light meals for at least 6h and from fried or fatty foods and meat for at least 8h[2].

While these guidelines provide recommendations for clear fluids and solid food, they do not mention enteral feeding, and we were unable to find any published studies on gastric emptying time after enteral feeding. This is likely why the current practice is to apply the same fasting time for solid food to enteral formula, but we expected that research could provide evidence for a shorter fasting time.

The results of our study indicate that gastric emptying time was 2 to 4h for fat-free oligomeric formula, and 3 to 5h for both fat-containing oligomeric formula and salted rice balls. Although the results of Study 1 and Study 2 cannot be directly compared, they may be somewhat helpful because the results for clear fluid were nearly identical. These differences in gastric emptying time are likely due to differences in nutrient composition and caloric concentrations.

In the regulation of gastric emptying, the pyloric antrum, pylorus, and upper duodenum function as a structural unit: contraction of the pyloric antrum is followed by contraction of the pylorus and duodenum. Contraction of the pylorus prevents solids from flowing into the duodenum and mixes and pulverizes gastric contents, which are carried into the duodenum gradually[6]. Nutrients in ingested food and the various properties of those nutrients can delay gastric emptying time[7]. Hunt *et al.,*[8] found that various types and concentrations of acids[9], saturated fatty acids[10], glucose solution, or potassium chloride solution[11] administered to healthy volunteers either orally or by gastric tube suppressed gastric emptying. Their results suggested the presence of three types of receptors that respond specifically to pH[9], fatty acids[10], and osmolality[11].

Meeroff *et al.,*[12] placed a gastric tube or dual-lumen duodenal tube in healthy volunteers, then injected liquid test meals of various osmolalities through the gastric tube and perfused solutions of sodium chloride or mannitol at various osmolalities through the duodenal tube. They showed that the gastric emptying time is modified by the osmolality of the duodenal perfusate. In that study, they also passed the perfusate tube beyond the ligament of Treitz and perfused the jejunum with perfusate of various osmolalities, but found that perfusion of the jejunum with high-osmolality perfusate did not slow gastric emptying. These results suggest that osmoreceptors are located in the duodenum and not the stomach or jejunum.

Lobo *et al.,*[13] found that gastric emptying time is more strongly influenced by nutrient composition than by general physical characteristics such as volume, osmolality, viscosity, or density. Hunt *et al.,*[14] and Calbet *et al.,*[7] found that the ingestion of food and drink with high caloric concentrations slows gastric emptying.

The fat-free oligomeric formula we used in this study (two 200-ml bottles of Peptino®) contained over twice as many carbohydrates as the clear fluid (500-ml sports drink), plus amino acids, and consequently contained over three times as many calories (Table 2). The fat-containing oligomeric formula (two 200-ml bottles of Peptamen Standard®) contained over three times as many carbohydrates as the clear fluid (400-ml sports drink), plus amino acids and fat, and consequently contained over six times as many calories (Table 3). The volume, osmolality, viscosity, and density of the fat-free oligomeric formula (Peptino®) and the fat-containing oligomeric formula (Peptamen Standard®) used in this study did not differ significantly, at 400 versus 400mL, 500 versus 520mOsm/L, 6 versus 7mPa-s, and 1.1 vs 1.1 kg/m^3. Our results also support the findings of Lobo *et al.,* and Hunt *et al.,* that high caloric concentrations of food and drink are associated with gastric emptying[13,14].

Table 2: Composition of drinks in Study 1:

	Fat-free oligomeric formula (Peptino®) 200ml × 2 packs	**Clear fluid (sports drink) 500ml**
Carbohydrates (g)	85.6	31
Amino acids (g)	14.4	-
Osmolarity (mOsm/L)	500	-
Energy (kcal)	400	125

Table 3: Odds ratios and 95% confidence intervals for length of ICU stays:

	Clear fluid (sports drink) 400ml	Fat-containing oligomeric formula (Peptamen® Standard) 200ml × 2 packs	Salted plain rice ball 100g × 2 pieces
Carbohydrates (g)	25	75	92
Amino acids (g)	-	10.5	3.4
Fat (g)	-	12.5	0.5
Osmolarity (mOsm/L)	401	520	-
Energy (kcal)	100	600	400

In Study 2, we included a control group given solid food. This was because the fat in fat-containing oligomeric formula might have further slowed gastric emptying time, to where the gastric emptying time would be comparable to that for solid foods.

The results of our study may be useful for patients who are receiving enteral formula via a feeding tube because they are unable to ingest food orally for any of various reasons, including patients in the intensive care unit.

Our study has some limitations. First, all of the study participants were healthy men, and some studies suggest that gastric emptying time is longer in women than men due to factors such as progesterone[15]. Many other factors may also delay gastric emptying time, including obesity, digestive disorders, diabetes, and labor pain relief. However, the ESA guidelines for fasting suggest that such patients can follow the same guidelines as healthy individuals because these factors only slightly slow gastric emptying[3].

Second, this study used ultrasonography as a minimally invasive and simple method to determine gastric emptying time, but this may not accurately reflect actual gastric emptying time. Scintigraphy is considered the gold standard for determining intragastric volume, with MRI considered equivalent[16-19]. However, some studies have shown that ultrasonography is not significantly different from scintigraphy[20,21]. For example, Perlas *et al.,*[22] studied ultrasonographic determination of intragastric volume and suggested that the stomach can be considered near empty when the CSA in the right lateral decubitus position is $\leq 4cm^2$. Ultrasonography is prone to measurement error from technician-related and subject-related factors. In this study, scans were performed by a single observer to minimize measurement error as much as possible.

CONCLUSION

We evaluated gastric emptying time of fat-free oligomeric formula, fat-containing oligomeric formula, rice balls, and clear fluid by ultrasonography in men. Gastric emptying times for fat-free oligomeric formula (400 kcal/400 ml), fat-containing oligomeric formula (600 kcal/400 ml), rice balls (400 kcal/200 g), and clear fluid (100 kcal/400 ml) were 3.5 [3-4] h, 4.5 [3-5] h, 4 [4-4.25] h, and 1.5 [1-2] h.

This suggests that calories may more strongly affect gastric emptying time than physical properties. Many patients, including those in the intensive care unit, receive enteral formula via a feeding tube because they are unable to ingest food orally for various reasons, and preoperative fasting times for such patients were previously unknown. However, our results indicate that the liquid nature of enteric formula does not necessarily lead to faster gastric emptying than solid food; rather, higher calorie content is associated with slower gastric emptying.

LIST OF ABBREVIATIONS

ASA: American Society of Anesthesiologists; **CSA:** Cross-sectional area; **ERAS:** Enhanced Recovery after Surgery; **ESA:** European Society of Anaesthesiology; **JSA:** Japanese Society of Anesthesiologists; **MRI:** Magnetic Resonance Imaging; **ORT:** oral rehydration therapy.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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