

Does the menstrual phase affect gastric emptying? Prospective, observational study

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Abstract. – OBJECTIVE: Pulmonary aspiration of gastric content is a serious complication of anesthesia. It is unclear what effects different parts of the menstrual cycle have on how long it takes for the stomach to empty. This prospective observational study assessed the relationship between menstrual cycle phases and gastric emptying using ultrasonography (USG) in volunteers of reproductive age.

PATIENTS AND METHODS: Between days 8-10 of the menstrual cycle in the follicular phase and days 18-20 of the luteal phase, a total of 24 healthy volunteers received four stomach USG procedures. In both phases, the gastric antrum was evaluated with USG in the right lateral decubitus position after fasting for 10 hours, followed by 2 hours of fasting after liquid intake and 6 hours of fasting after solid food intake. The gastric content, gastric antrum area, and estimated gastric volume determined whether the stomach was full or empty.

RESULTS: A full stomach was detected in 8 (8.3%) out of 96 measurements performed on the volunteers. After liquid food intake, a full stomach was detected in 2 subjects in the luteal phase, while all the subjects had an empty stomach during the follicular phase ($p=0.500$). After solid food intake, a full stomach was detected in 6 subjects in the luteal phase, and again, all subjects had an empty stomach during the follicular phase ($p=0.031$).

CONCLUSIONS: Ultrasound assessment of gastric volume in volunteers of reproductive age has shown that gastric emptying of solid foods is slowed during the luteal phase of the menstrual cycle.

Key Words:

Gastric emptying, Progesterone, Menstrual cycle, Gastric ultrasonography.

depending on the patient's clinical history and pre-operative pathology^{1,2}. Despite its highly variable clinical spectrum, pulmonary aspiration is a significant cause of morbidity and mortality^{1,3}. Up to 47% of patients with pulmonary aspiration have developed pneumonia⁴. The amount of aspirated stomach contents is a major risk factor for the development of pulmonary aspiration, which is associated with poor clinical results⁵. There are universal pre-operative fasting protocols for all elective surgical procedures to guarantee an "empty" stomach during the induction of anesthesia⁶. Patients undergoing emergency surgery, those who are unable to fast, those experiencing severe pain, and those who may have delayed gastric emptying due to several factors associated with a disease-related surgical indication are not included in these guidelines (e.g., intestinal obstruction)^{7,8}. Delay in gastric emptying has also been linked to Parkinson's disease⁹, diabetes mellitus, gastroesophageal reflux disease, dyspepsia, and long-term opioid use¹⁰. These patients are more likely to have a full stomach despite the fasting durations specified in the recommendations, increasing the risk of aspiration even in the planned surgical setting. To evaluate the potential for pulmonary aspiration, it would be helpful to undertake a non-invasive assessment of the patient's stomach contents before the induction of anesthesia¹¹.

Various methods, such as X-ray imaging, magnetic resonance imaging, and radionuclide imaging, are available to evaluate gastric volume and contents in clinical practice. Nevertheless, all these methods have disadvantages, such as high cost, radiation exposure, and discomfort. Gastric ultrasound (USG) is a simple, rapid, and non-invasive bedside diagnostic test that provides a qualitative and quantitative evaluation of gastric contents^{2,12}. Gastric USG allows anesthesiologists to estimate gastric fluid volume, determine the gastric content type (solids, thick liquids, clear liquids), and predict "full stomach" and "empty stomach". In addition, the information obtained from the gastric

Introduction

Patients undergoing general anesthesia risk a dangerous perioperative complication known as pulmonary aspiration of stomach contents, which can occur anywhere from 0.1% to 19% of patients,

USG can be used to determine the optimal timing for elective procedures, anesthesia selection, and the airway management approach¹³.

Although the effect of gender on gastric emptying in a healthy population is controversial, gastric emptying of solid foods may be slower in women¹⁴⁻¹⁷. Females have been found¹⁵ to have shorter migrating motor complex durations using ambulatory antroduodenal manometry. The mechanisms underlying these differences are not fully understood, and there are conflicting reports in the literature. A study¹⁶ of duodenojejunal motility, for instance, found that follicular-phase women have a motor activity comparable to that of males. Women's postprandial antral stomach contractile activity was lower than men's during the follicular phase, as demonstrated by Knight et al¹⁷. Since the gastric emptying rate for solid foods decreases linearly as the menstrual cycle progresses towards the luteal phase (days 19-28), the fact that the gastric emptying is slower in females than in males may be attributed to the phase of the menstrual cycle at the time of the research^{18,19}. However, despite many surgical procedures performed on millions of patients of reproductive age, the results of studies investigating the relationship between gastric emptying and menstrual cycle phases are inconsistent. This study aimed to evaluate the relationship between menstrual cycle phases and gastric emptying after liquid and solid food ingestion using USG in healthy female volunteers of reproductive age.

Patients and Methods

Design and Setting

Approval for this prospective observational study was granted by the Ethics Committee of University of Health Sciences, Hamidiye Scientific Research Ethics Committee (decision No.: 22/125, dated: March 03, 2022). The study protocol was registered in the international database ClinicalTrials.gov (registration No. NCT05407558). All procedures were in accordance with the Helsinki Declaration²⁰, and the Consolidated Standards of Reporting Trials (CONSORT) statement²¹.

Patient Enrollment

This study was conducted on healthy female volunteers in the Department of Anesthesiology and Reanimation, Health Sciences University Konya Training and Research Hospital, between July 2022 and August 2022. All participants in the research gave their informed, written agreement to partici-

pate. Evaluations of gastric emptying were made using USG in both phases of the menstrual cycle. The volunteers were females aged 18 and 40 with a regular menstrual cycle for at least six months. The study exclusion criteria were pregnancy, the presence of gastric problems, the use of anticholinergics or opioids, a diagnosis of hypothyroidism or diabetes mellitus, smoking, or oral contraceptives.

Study Protocol

Each study participant was questioned about the first date of the last menstrual period and the duration of the menstrual cycle, and the day of the menstrual phase was calculated. The volunteers included in the study were evaluated twice in total at 8-10 and 18-20 days of their cycle²². The evaluations were made after at least 10 hours of fasting.

For liquid food intake

First, gastric emptying after liquid food intake was evaluated. Gastric evaluation with USG was performed on the volunteers 2 hours after the ingestion of 400 ml of water²³.

For solid food intake

Secondly, gastric emptying after solid food intake was evaluated. Gastric evaluation with USG was performed on the volunteers at the 6th hour after taking a light meal (toast and 200 ml tea)^{6,8}. These evaluations were made on the same subjects, in both follicular and luteal phases, a total of 4 times. The study protocol diagram is shown in Figure 1.

Ultrasound Examination

None of the images were collected during peristaltic contractions; instead, they were all obtained by evaluating the stomach antrum at rest. All sonographic tests were carried out by the same radiologist, who was both experienced in abdominal ultrasound and blinded to the volunteer's diet. In accordance with the instructions, the evaluation was performed in the right lateral decubitus position using a typical 4 MHz convex probe (ESAOTE brand MyLabFive-EsaoteEurope BV Philipsweg 1 6227 AJ, Maastricht, Netherlands) and a curved array, low-frequency transducer (2-5 MHz, 60 mm).

The property of stomach contents (liquid or solid) was determined, and the antrum cross-sectional area (CSA) was calculated⁸. Estimated gastric volume was calculated according to the calculated CSA²⁴. The antral cross-sectional area was determined by utilizing two diameters that were perpendicular to one another in addition to the formula that determines the area of an ellipse:

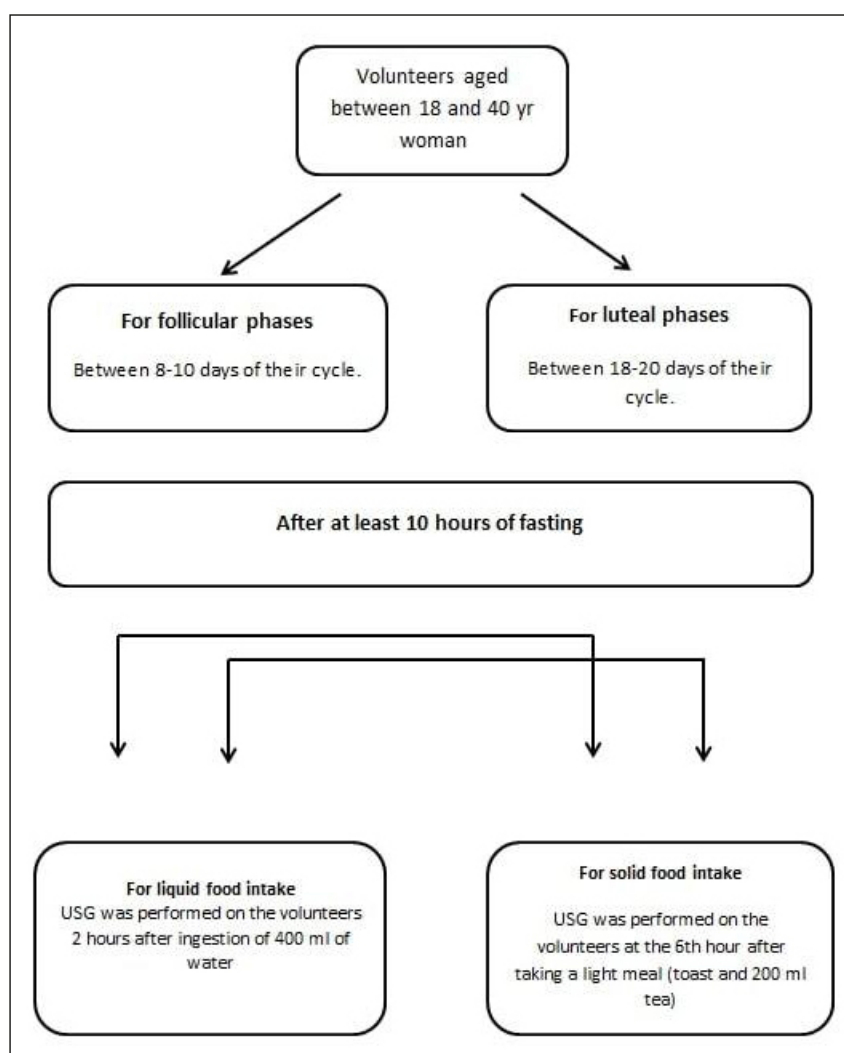


Figure 1. The study protocol diagram.

- $CSA = [\text{antero-posterior diameter (AP)} \times \text{craniocaudal diameter (CC)} \times \pi] / 4$
- Gastroscopic fluid assessment was calculated using the previously validated formula:
- $GV \text{ (ml)} = 27.0 + 14.6 \times \text{right-lat CSA} - 1.28 \times \text{age}^{24}$.

When there was less than 1.5 mLkg^{-1} of fluid in the stomach, it was considered empty, and when there was more than 1.5 mLkg^{-1} of fluid, it was regarded full⁸.

The primary outcome was that gastric ultrasonography, 6 hours after eating solid food, showed that more women in the luteal phase than in the follicular phase had full stomachs. The secondary outcome was a greater prevalence of full stomach in the luteal phase than in the follicular phase when measured by gastric ultrasonography at 2 hours after liquid food intake.

Sample Size

Using McNemar's test and the MedCalc version 20.027 (Ostend, Belgium) software, with $\alpha=0.05$, a one-sided confidence interval, and 80% power, a power analysis was conducted using data from ten volunteers. The sample size was determined to be 24 volunteers.

Statistical Analysis

Statistical Package for the Social Sciences version 22.0 (SPSS, IBM Corp., Armonk, NY, USA) was used to perform statistical analyses on the research data. The Kolmogorov-Smirnov test was used to check for data normality. Categorical variables were expressed as number (n) and percentage (%), while continuous variables were reported as mean, standard deviation (SD), or median (25th-75th percentile) values depending on the distribu-

tion status. When testing continuous variables, the Independent Samples *t*-test was used if the test's parametric assumptions were fulfilled. Otherwise, the Mann-Whitney U test was used. The Paired Sample *t*-test was used to change the dependent variables at two separate periods. The Pearson Chi-square test and McNemar's test were used to compare categorical data. We used the Pearson's correlation test if the conditions were satisfied for continuous variables. Otherwise, the Spearman's rho correlation test was used. Statistical significance was assumed to be at the $p < 0.05$ level.

Results

A total of 96 measurements were made on 24 volunteers participating in the study. The volunteers' mean height was 162.88 ± 6.38 cm, mean weight was 60.83 ± 6.97 kg, mean BMI was 22.97 ± 2.45 kgm^{-2} and mean age was 25.67 ± 4.45 years.

The CSA values of the volunteers were higher in the luteal phase than in the follicular phase. This change between phases was not statistically significant after the liquid food intake but was statistically significant after the solid food intake ($p = 0.243$ and $p = 0.025$, respectively). The GV (ml) measurement values were higher in the luteal phase than in the follicular phase. This difference between phases was not statistically significant after the liquid food intake but was statistically significant after the sol-

id food intake ($p = 0.367$ and $p = 0.001$, respectively). Detailed information on all the measured CSA and GV (ml) values is given in Table I.

After the liquid food intake, 2 (8.32%) subjects had a full stomach in the luteal phase, while no volunteer had a full stomach in the follicular phase. This change between the phases in volunteers was not statistically significant ($p = 0.500$). The gastric evaluation of the volunteers after liquid food intake is shown in Table II. After the solid food intake, 6 (24.96%) volunteers had a full stomach in the luteal phase, and no subject had a full stomach in the follicular phase. This change between phases after the solid food intake was not statistically significant ($p = 0.031$). The gastric evaluation of the volunteers after solid food intake is shown in Table III. None of the gastric evaluations detected any particulate content in any subject.

Discussion

This study investigating the relationship between menstrual cycle phases and gastric emptying detected a full stomach in 8.33% of the measurements despite following preoperative fasting guidelines. It was also found that more volunteers had a full stomach after the solid food intake in the luteal phase compared to the follicular phase, and the difference between the phases was statistically significant.

Table I. CSA and GV scores of volunteers.

Department		CSA (cm ²)	GV (ml)
For liquid food intake	Follicular phases, mean±(SD)	4.57±1.50	62.75±24.50
	Luteal phases, mean±(SD)	5.06±1.52	68.97±25.64
	<i>p</i> -value	0.243	0.367
For solid food intake	Follicular phases, mean±(SD)	4.94±2.00	61.64±18.54
	Luteal phases, mean±(SD)	6.12±2.09	82.84±31.23
	<i>p</i> -value	0.025*	0.001**

* $p < 0.05$, ** $p < 0.01$. Paired-Samples *t*-test was used.

CSA: Cross-Sectional Area, GV: gastric volume, SD: Standard Deviation.

Table II. Evaluation of stomach fullness after liquid food intake.

		Luteal phases	
		Empty stomach	Full stomach
Follicular phases	Empty stomach	22	2
	Full stomach	0	0

McNemar's test was used.

Table III. Evaluation of stomach fullness after solid food intake.

		Luteal phases	
		Empty stomach	Full stomach
Follicular phases	Empty stomach	18	6
	Full stomach	0	0

McNemar's test was used.

Changes in sex steroid serum levels may affect gastrointestinal smooth muscle. Lower esophageal sphincter (LOS) pressure values have been recorded during the third trimester of pregnancy²⁵ and with oral administration of progesterone-containing birth control tablets²⁶. *In vivo*²⁷ and *in vitro*²⁸ investigations support this observation. *In vitro* inhibitory impact of steroids on gallbladder smooth muscle²⁹, especially with high blood progesterone levels, supports decreased gallbladder function during pregnancy³⁰ and the luteal phase of the menstrual cycle^{31,32}. In addition, a full feeling in the stomach after eating solid food was shown to be much higher in the luteal phase of the menstrual cycle when progesterone levels were high than in the follicular phase. These findings agree with Gill et al¹⁹, who found that solid-phase indicators empty more slowly during the luteal phase than during the follicular phase. They also found that decreased stomach emptying of solid meals correlates with higher blood progesterone levels.

Progesterone inhibits distal gastric smooth muscle contractility *in vitro*³³⁻³⁵. Myoelectric slow waves determine distal stomach smooth muscle contractions with their frequency, velocity, and direction of propagation³⁴. Progesterone decreases stomach slow waves, which may impact solid food emptying³⁶. The current study's result shows that liquid food emptying is not changed by the menstrual cycle, and this is consistent with Wald et al²², showing that variations in orofecal transit are mostly related to changes in small intestine transit rather than stomach emptying.

Differences in the effects of pregnancy or the menstrual cycle on the stomach in previous studies^{18,19,22,23} may be due to different test meals with distinct calories and nutrient composition, or different techniques used to measure gastric emptying. Several techniques, such as the absorption of paracetamol, a radiolabeled food, the dilution of polyethylene glycol, electrical impedance tomography, and aspiration of stomach contents, have been reported⁸ to measure gastric volume. On the other hand, these procedures are difficult to implement during the perioperative period because they are complicated, invasive, time-consuming,

and demand specialized equipment, personnel, and knowledge³. Bedside USG is another modality that may be utilized to determine stomach volume. It is uncomplicated, easily accessible, non-invasive, and straightforward to conduct, and it has demonstrated dependability amongst observers³⁷. In addition, due to prominent anatomical landmarks, the stomach antrum may be precisely measured. The calculated antrum cross-sectional area is linearly correlated with gastric volume, as confirmed by routine gastroscopy measurement in adults and nasogastric tube aspiration in children⁸. Quantitative or semi-quantitative approaches based on measuring the gastric antrum can be used to determine the stomach volume before surgery. To estimate stomach volumes, these methods employ position-specific validated formulae that use the antral section measurements as inputs^{8,10}. In addition, mathematical models or scales based on the observation of gastric fluid in various postures can be used to determine gastric fluid volume^{24,37,38}. In this study, we measured the antral cross-sectional area in the right lateral decubitus (RLD) position. We used the Perlas qualitative rating scale to determine whether or not participants' stomachs were full or empty²⁴. 25% of the participants, although adhering to the existing preoperative fasting rules for solid foods, were found to have a full stomach in the luteal phase, indicating a significant risk of regurgitation and pulmonary aspiration while under general anesthesia. As a result, rapid sequence induction and tracheal intubation are recommended for patients who require general anesthesia but have recently eaten.

Limitations

This study had several limitations. Firstly, stomach content was evaluated using only a non-invasive tool and was not directly measured. Since the goal of this study was to determine whether the stomach was still full at the end of the time specified in the guidelines, sequential measurements were not performed, so the rate of gastric emptying in these subjects is not clear. Second, to determine the effect of the menstrual phase alone, the study population was comprised

of healthy volunteers with no comorbidities or risk of delayed gastric emptying. This risk could be caused by a potential reduction in gastrointestinal peristalsis associated with acute stress and pain, which could be made worse by opioid analgesics³⁹⁻⁴¹. Therefore, the relevance of these results for patients with severe systemic disease or requiring emergency surgery is unclear.

Conclusions

In this study, sonographic gastric measurements in female volunteers of reproductive age indicated the possibility of unexpected delayed gastric emptying in the luteal phase, which is a risk factor for poor outcomes such as pulmonary aspiration of gastric contents. Therefore, preoperative gastric content evaluation during the luteal phase on women of reproductive age is recommended, especially in the presence of additional risk factors.

Conflicts of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

Not applicable.

Ethics Approval

Approval for this prospective observational study was granted by the Ethics Committee of University of Health Sciences, Hamidiye Scientific Research (decision No.: 22/125, dated: March 03, 2022). In addition, the study protocol was registered in the international database ClinicalTrials.gov (registration No. NCT05407558).

Informed Consent

All participants in the research gave their informed, written agreement to participate.

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