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## Association of Gastric Emptying with Postprandial Appetite and Satiety Sensations in Obesity

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### Abstract

**Introduction:** Satiety, defined as the duration of the sensation of fullness, is usually measured by validated visual analog scales (VAS) for appetite. Gastric function plays a key role in food intake regulation. However, the association between gastric emptying (GE) and VAS-appetite is unknown.

**Methods:** In this cross-sectional study, 134 participants [age=39±0.8 years, BMI=38±0.5 kg/m<sup>2</sup>, 67% females] completed simultaneous measurements of GE and VAS-appetite. After a 320kcal meal, GE was measured by scintigraphy and appetite by validated 100mm VAS for 240 min. Then, in the same day, satiation, defined as calories consumed to terminate meal, and measured by *ad libitum* meal. Percent of meal retention in the stomach, VAS area under curve (AUC<sub>0–240min</sub>), and overall appetite score (OAS) were calculated. Pearson correlation ( $\rho$ ) determined the association of GE with VAS-appetite and satiation. Appetite components were also analyzed by quartiles based on GE<sub>120min</sub>.

**Results:** GE<sub>120min</sub> was correlated with sensation of VAS-hunger<sub>AUC(0–240min)</sub> ( $\rho=0.24$ ,  $p=0.004$ ), fullness<sub>AUC(0–240min)</sub> ( $\rho=0.16$ ,  $p=0.05$ ), and OAS<sub>AUC(0–240min)</sub> ( $\rho=0.20$ ,  $p=0.02$ ). Patients with rapid GE<sub>120min</sub> had a mean increase in VAS-hunger<sub>AUC(0–240min)</sub> by 32 mm/min (15.62%,  $p=0.03$ ) compared to normal/slow GE<sub>120min</sub>.

**Conclusions:** GE is associated with the sensations of appetite, and rapid GE is associated with increased appetite, which may contribute to weight gain.

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**Clinical trial registration:** The studies reported here constitute baseline measurements prior to inclusion in the therapeutic trial NCT03374956.

## Keywords

Eating behavior; hunger; satiety; stomach; gastric physiology; calorie consumption

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## INTRODUCTION

The control of food intake is a regulated and complex process, which is highly influenced and often overridden by hedonic components(1, 2). The stages of food intake regulation are hunger, satiation, and satiety. Hunger represents the sensation that encourages the initiation of food consumption. Satiation is the sensation of fullness during a meal that aids in inducing the termination of a meal(2). Satiety is the period of time in which the fullness sensation persists(3). These different stages are regulated by homeostatic and hedonic cues that coalesce to control eating behavior.

The homeostatic regulation is driven by the brain-gut-adipose tissue axis. The hunger system in the hypothalamus is always turned “on”(4, 5). Satiety starts when an individual has reached satiation, terminated the meal, and the hunger system is in “off” mode. Peripheral signals, mainly from the distal gut, adipose tissue, and visceral afferent vagal fibers communicate with the brainstem and hypothalamus to signal this sensation of fullness, slow down the upper gut motor functions, enhance nutrient digestion, and maximize calorie absorption. This slowing of gastric emptying and reduced upper small bowel motility is mediated by the ileal brake(6–8). Gastric emptying is associated with caloric intake during the next meal(9, 10). However, it is a complex process that varies depending on the consistency, volume, macronutrient, and caloric content of the food consumed(11, 12).

The importance of satiety in food intake regulation and related disorders such as obesity has led researchers and clinicians to develop reliable and validated measurements of satiety, reviewed in detail elsewhere(13). The most commonly-used satiety tests are the appetite rating scales; however, other measurements are more complex, such as blood biomarkers (e.g. satiety gut hormones)(13), gastric functions testing (e.g. gastric emptying, volume or distention)(5), and functional brain magnetic resonance imaging(14). The appetite rating scales are commonly measured using 100-mm visual analog scales (VAS) for hunger, fullness, satisfaction, and desire to eat. The overall appetite score (OAS) is calculated as  $OAS = [satiety + fullness + (100 - hunger) + (100 - desire\ to\ eat)]/4$ , where 100 indicates more appetite and 0 indicates less appetite(15, 16). Although the appetite rating by VAS is widely adopted, the test has a moderate reproducibility (20–60%) and high inter-individual variability(17, 18). Furthermore, a recent meta-analysis of 462 scientific manuscripts showed that appetite scores do not reliably predict energy intake(19). Gibbons et al., explain these limitations suggesting that “subjective sensations do not provide the full picture of appetite control and other variables are contributing to satiety”(13).

In pursuit of more objective tools to measure satiety, gastric emptying has been used as an alternative test for postprandial satiety(9, 20). In particular, gastric emptying has been used to study subsequent food intake(9, 21), fasting and postprandial ghrelin(22, 23), and weight loss outcomes with satiety-reducing interventions, e.g. exenatide(24), liraglutide(21, 25), and intragastric balloons(26–28). The gold standard test for measuring gastric emptying

is scintigraphy with a standard radiolabeled meal, which is reproducible (coefficient of variation 9–25%) over short-, intermediate-, and long-term in healthy volunteers(29). Furthermore, gastric emptying is accelerated in obesity when compared to healthy weight controls(20), and patients with faster gastric emptying gain more weight than those with normal gastric emptying when followed prospectively for 4 years(30).

However, the association between GE and appetite symptoms measured simultaneously after ingesting a standard meal has not been studied. Thus, it is key to understand whether GE correlates with appetite sensations in order to be used as markers for postprandial satiety. We hypothesize that percentage of solids emptied during the GE test is positively associated with the sensation of fullness in the assessment of appetite. Therefore, this cross-sectional study aimed to evaluate the correlation between gastric emptying of solids measured simultaneously with a visual analog scale for appetite, and satiety sensations in participants with obesity.

## METHODS

### Participants

A total of 134 subjects between 18 and 65 years old, with obesity (BMI >30 kg/m<sup>2</sup>) and no evidence of active psychiatric symptoms, eating disorders (specifically, bulimia), or alcohol use disorders were prospectively enrolled as part of [ClinicalTrials.gov NCT03374956](https://clinicaltrials.gov/ct2/show/study/NCT03374956) trial. Here we report the baseline measurements prior to inclusion into the trial, which studied the effect of anti-obesity medication based on phenotypes. The study was approved by the Mayo Clinic Institutional Review Board (IRB # 17–003449) and all participants gave written informed consent following a thorough explanation of the study details. Women of childbearing potential had a negative pregnancy test within 48 hours before testing. All the studies were performed at the Mayo Clinic Clinical Research Trials Unit (CRTU) after an 8-hour fasting period. The exclusion criteria were history of bariatric procedures, use of medications that may alter gastrointestinal motility, appetite, or absorption (e.g. orlistat, neuromodulatory agents, etc.) within the last 6 months, and history of hypersensitivity to the components of the study material or meals.

### Study Visit Overview

Participants reported to the Research unit between 6 am and 8 am. All participants confirmed overnight fasting status with at least 8 hours from the last meal and completed measurements of satiety and satiation on the same day. Participants underwent a body composition scan by dual energy X-ray absorptiometry (DEXA) at arrival to the research unit. After a standardized breakfast, satiety was measured concurrently with gastric emptying of solids by scintigraphy and appetite VAS. Satiation was assessed by quantification of total calories consumed after an *ad libitum* meal 240 minutes after the standardized breakfast (Figure 1). Both meals (i.e. standard breakfast and *ad libitum* meal) were provided in the Gastroenterology Lab of CRTU, participants were isolated from each other, and external visual food cues were minimized.

## Measurements of Satiety

A standard breakfast of 320kcal, 30% fat meal consisting of two  $^{99m}\text{Tc}$ -radiolabeled eggs, toast, and 80 ml of skim milk was given to participants. The appetite rating scale was measured using a validated, standard, 100mm appetite VAS for hunger, and fullness(17, 31). Appetite VAS was assessed 15 minutes before the standard meal, after meal termination, then every 30 minutes for the first 120 minutes, and at 240 minutes for a total of 7 assessments. Following the last appetite VAS, participants were provided an *ad libitum* meal (see details below). Gastric emptying of solids was measured using the gold standard scintigraphy technique of two  $^{99m}\text{Tc}$ -radiolabeled eggs that were included in the standardized breakfast. Images were acquired after breakfast termination, then every 15 minutes for the first 60 minutes, and at 60, 90, 120, 180, and 240 minutes (20, 29, 32).

## Measurement of Satiation

The *ad libitum* meal was performed 240 minutes after standard breakfast and included *all you can eat* lasagna, vanilla pudding, and skim milk(20). Participants were invited to eat as much as they could until reaching maximal fullness. During the feeding paradigm there was no time limit to consume the meal. The *ad libitum* meal included: vegetable lasagna [Stouffers®, Nestle USA, Inc, Solon, OH; nutritional analysis of each 326g box: 420kcal, 17g protein (16% of energy), 38g carbohydrate (37% of energy), and 22g fat (47% of energy)]; vanilla pudding [Hunts®, Kraft Foods North America, Tarrytown, NY; nutritional analysis of each 99g carton: 130kcal, 1g protein (3% of energy), 21g carbohydrate (65% of energy), and 4.5g fat (32% of energy)]; and skim milk [nutritional analysis of each 236mL carton: 90kcal, 8g protein (36% of energy), 13g carbohydrate (64% of energy), and 0g fat]. The total amount (g and kcal) of food consumed and the kcal of each macronutrient at the *ad libitum* meal were analyzed by a registered dietitian, using validated software (ProNutra 3.0; Viocare Technologies Inc, Princeton, NJ).

## Study Endpoints

Prior studies in healthy controls and obesity show about 50% of meal retained in the stomach at 90–120 minutes(20, 29, 32); therefore, this is the most relevant time period to assess the relationship between gastric emptying and VAS appetite.

## Statistical Analysis

Data are shown as mean and one standard error of the mean (SEM) unless otherwise noted. Student T-test was used to compare differences in continuous variables by gender. The primary analysis was the Pearson correlation ( $\rho$ ) of the percentage of meal retention at 120 minutes ( $\text{GE}_{120\text{min}}$ ) during the GE study, with concurrent VAS appetite (33, 34). Our secondary analysis was the Pearson correlation of GE and VAS appetite at each of the a priori specified time points; and the correlation of GE and VAS appetite with the number of calories consumed at the *ad libitum* meal. The analysis was adjusted for age, gender, BMI and percentage of body fat. An additional analysis was performed by quartiles using the  $\text{GE}_{120\text{min}}$ ; Q1 was defined as the rapid GE group and the remaining patients in Q2-Q4 were defined as having normal/slow GE. Area under the curve (AUC) was calculated using all VAS time points ( $\text{AUC}_{0-240\text{min}}$ ). Plots and statistical analyses were performed using JMP®,

Version 14.1.0. SAS Institute Inc., Cary, NC, 1989–2019. Two-tailed P-values 0.05 were considered statistically significant.

## RESULTS

### Demographics and Participant Characteristics

A total of 134 participants with obesity completed the GE, satiety, and satiation tests. Participant characteristics were (mean  $\pm$  SEM): age  $39 \pm 0.8$  years, BMI  $38 \pm 0.5$  kg/m<sup>2</sup>, and 67% female (Table 1).

### Measurements of Gastric Emptying, Appetite, and *Ad libitum* meal

The mean GE  $T_{1/2}$  was  $117.3 \pm 2.3$  minutes and the  $GE_{120\text{min}}$  was  $46 \pm 1.3\%$ . The VAS AUC from 0–240 minutes for hunger ( $\text{hunger}_{\text{AUC}(0-240\text{min})}$ ) was  $209.5 \pm 6.4$  mm/min, was  $168.3 \pm 6.2$  mm/min for fullness ( $\text{fullness}_{\text{AUC}(0-240\text{min})}$ ), and  $164.4 \pm 5.3$  mm/min for VAS OAS ( $\text{OAS}_{\text{AUC}(0-240\text{min})}$ ). The mean VAS at 120 min ( $\text{VAS}_{120\text{min}}$ ) was  $51.7 \pm 2$  mm for hunger,  $38.5 \pm 2$  mm for fullness, and  $42.4 \text{ mm} \pm 1.8$  for OAS. The mean *ad libitum* meal intake was  $905.1 \pm 26.5$  kcal. The mean macronutrient intake during the *ad libitum* meal was protein  $22.7 \pm 0.2\%$ , fat  $20.6 \pm 0.2\%$ , and carbohydrate  $56.7 \pm 0.2\%$  (Table 1). The coefficient of variation was 33% for  $GE_{120\text{min}}$  and 49% for  $\text{VAS OAS}_{120\text{min}}$ .

### Effect of Gender on measurements of Gastric Emptying, VAS Appetite, and Satiation tests.

There were statistically significant differences when analyzed by gender (Table 1). The GE was significantly slower in females with a difference of  $-11.3\%$  (95% confidence interval [CI],  $-16.1$  to  $-6.5$ ;  $p < 0.0001$ ),  $-12.6\%$  (95% CI,  $-17.9$  to  $-7.17$ ;  $p < 0.0001$ ),  $-9.9\%$  (95% CI,  $-13.8$  to  $-6$ ;  $p < 0.0001$ ), and  $-5.4\%$  (95% CI,  $-7.3$  to  $-3.4$ ;  $p < 0.0001$ ) at 90, 120, 180, and 240 min, respectively. VAS scores were significantly lower in females at 90 minutes, with a difference of 10.9 mm (95% CI, 2.9 to 18.9;  $p = 0.008$ ) for hunger, and higher for fullness with a difference of  $-9.3$  mm (95% CI,  $-17.6$  to  $-1.07$ ;  $p = 0.03$ ). VAS OAS was significantly higher in females at 120 minutes, with a  $-7.2$  mm (95% CI,  $-14.1$  to  $-0.35$ ;  $p = 0.04$ ). We did not observe significant differences in  $\text{VAS}_{\text{AUC}(0-240\text{min})}$  for hunger, desire to eat, fullness, or satisfaction when analyzed by gender. Total kcal consumed during the *ad libitum* meal were significantly higher in males with a difference of 299 kcal (95% CI, 182 to 415.8;  $p < 0.0001$ ). There was no difference in the percentage of macronutrient intake between females and males.

### Relationship between Gastric emptying and Appetite sensations

GE, hunger, and fullness curves are provided in Figure 2. Figure 2 demonstrates the interaction of the gastric emptying percentage with the decrease in fullness and the increase in hunger after a standard breakfast.  $GE_{120\text{min}}$  positively correlated with VAS Fullness ( $\text{Fullness}_{\text{AUC}(0-240\text{min})}$ ) ( $\rho = 0.16$ ,  $p = 0.05$ ), VAS OAS ( $\text{OAS}_{\text{AUC}(0-240\text{min})}$ ) ( $\rho = 0.20$ ,  $p = 0.02$ ) and VAS OAS ( $\text{OAS}_{120\text{min}}$ ) ( $\rho = 0.18$ ,  $p = 0.04$ ). A negative correlation was observed with  $GE_{120\text{min}}$  and VAS Hunger ( $\text{Hunger}_{\text{AUC}(0-240\text{min})}$ ) ( $\rho = -0.24$ ,  $p = 0.004$ ), and VAS Hunger ( $\text{Hunger}_{120\text{min}}$ ) ( $\rho = -0.22$ ,  $p = 0.01$ ) (Figure 3). The correlation between  $GE_{120\text{min}}$  and sensation of appetite remained significant when adjusted for age, BMI and percentage of body fat.

### Relationship between Rapid Gastric Emptying and Appetite sensations

Rapid gastric emptying was defined as the fast  $GE_{120min}$  quartile per gender (Table 2). When compared to normal/slow GE, patients with rapid GE had a statistically significant higher sensation of VAS hunger:  $AUC_{0-240min}$  mean increase of 32 mm/min (15.6%,  $p=0.03$ ), VAS hunger at 120 minutes, mean increase of 8.7 mm ( $p=0.07$ ), and at 240 minutes, mean increase of 7.7 mm ( $p=0.008$ ) (Figure 4A). Conversely, we did not observe a significant difference between rapid and normal/slow GE in sensation of VAS fullness by  $AUC_{0-240min}$  mean decrease of 18 mm/min ( $p=0.21$ ), VAS fullness at 120 minutes mean decrease of 4.3 mm ( $p=0.34$ ), or at 240 minutes mean decrease of 2.7 mm ( $p=0.31$ ) (Figure 4B). Full details about demographics and VAS scores in rapid and rest GE groups are provided in Supplementary Table 1.

### Correlations between Gastric Emptying and VAS Appetite with Satiation measurements

Both VAS appetite sensations (i.e. hunger, fullness, desire to eat, satisfaction) and  $GE_{120min}$  were associated with the subsequent calories consumed at *ad libitum* meal.  $GE_{120min}$  and VAS OAS<sub>120min</sub> were negatively correlated with calories consumed in the *ad libitum* meal ( $\rho = -0.32$   $p=0.002$ ; and  $\rho = -0.38$ ,  $p<0.0001$ , respectively) (Figure 5A and 5B).

## DISCUSSION

Our studies, based on real-time, simultaneous measurements of gastric emptying and visual analog scale measurements of appetite, show that gastric emptying is associated with the sensations of appetite, and subsequent calorie intake at an *ad libitum* meal. These observations support the role of gastric emptying in homeostatic food intake regulation.

As expected, when the stomach is full after a meal, the sensation of hunger is lower and the sensation of fullness is higher; on the contrary, when the stomach is empty, the sensation of hunger is higher and fullness lower. This observation is very consistent among participants immediately after the standard breakfast and prior to the next meal. However, at 120 min postprandially, there is high variability in both the appetite sensation (49%) and the gastric emptying (33%). This variability represents the heterogeneity in satiety, which is defined as the duration of the sensation of fullness or return to hunger. Nonetheless, the high heterogeneity in the current tests should not hold back from proposing to use the 120 minutes postprandial time point as a key determinant and measurement of satiety. The biology of satiety can be evaluated either as the duration of fullness (VAS fullness), return to hunger (VAS hunger), or percent of meal retention at 120 minutes during the GE scintigraphy study.  $GE T_{1/2}$  has been previously associated with individual gastrointestinal symptoms such as early satiation, nausea, bloating, or the symptom complex of dyspepsia(9, 35–38); as well as being a biomarker of diseases such as gastroparesis(39).

In the pursuit of a gold-standard measurement of satiety, we must consider both the homeostatic and hedonic components in the regulation of food intake, and attempt to test homeostatic satiety mechanisms, while separating homeostatic from the hedonic mechanisms. The reported VAS measurements of the sensations of appetite are commonly regarded as subjective and are highly influenced by the hedonic component of feeding

behavior. Thus, it is important to identify and validate more objective measurements of satiety, which will not be affected by the emotional status of the individual. In our current study, we demonstrate that gastric emptying can be considered an objective measurement of satiety since it correlates in real-time with the sensation of appetite, and its subcomponents (hunger, desire to eat, fullness, satisfaction, and overall appetite) after a standard meal. As an example of the subjective measurement of the appetite score, a higher hunger sensation or lower fullness sensation does not correlate with acceleration or delay in GE. On the contrary, participants with rapid gastric emptying experienced a 15.6% increase in the sensation of hunger compared to participants with normal GE. This example illustrates how a homeostatic constituent, like GE, can serve as a more objective proxy of appetite sensation, non-influenced by the hedonic component of food intake regulation. These observations are important since the objective physiological assessment of GE may constitute a useful indirect tool of the homeostatic measurement of satiety – or return to hunger. Additionally, establishing an objective measurement of satiety such as GE at 120 minutes after a standardized meal may be valuable in physiologic and interventional studies where reproducibility between individuals and consistent measurements at different laboratories is crucial.

Gastric emptying is a critical factor in the gut-brain axis regulating food intake. GE correlates with hunger hormones like ghrelin (40) and satiety hormones like GLP-1 and PYY, all of which influence GE (41). Furthermore, rapid gastric emptying is associated with more weight gain in 4 years compared to normal gastric emptying in young adults(30), and physical activity accelerates gastric emptying and increases ghrelin(42). Moreover, the identification of rapid GE can help to individualize treatment strategies in patients with obesity to achieve better weight loss outcomes(43). Thus, in two pilot studies, we have shown that patients with obesity and rapid GE respond better to GLP-1 analogs, exenatide(24), and liraglutide(21). More recently, abnormal postprandial satiety – defined as rapid GE – was identified as a key phenotype in a novel obesity classification based on pathophysiological and behavioral traits(43). Furthermore, the classification was used to guide antiobesity pharmacotherapy in a 312 patient’s pragmatic trial and showed that patients treated with liraglutide and abnormal postprandial satiety had 2x more weight loss than patients with normal postprandial satiety(43). This suggests the clinical relevance of GE as an objective measurement of postprandial satiety.

The calorie intake of the next meal – or expected satiation – is influenced by the nutritional properties of the previous meal, homeostatic food intake signals, and learned behavior about expected satiation potential. The high impact of the psychological facet of food intake increases the difficulty of predicting calorie intake or appetite. A meta-analysis examining VAS appetite revealed the absence of a significant correlation between the VAS appetite scores and energy intake(19). In the current study of 134 patients, we have shown that both GE and VAS correlated with calorie intake in the subsequent meal.

### **Strengths and weaknesses:**

The reported study strengths are the large sample size, the tests performed simultaneously on the same day, in participants with obesity who had minimal or no comorbidities that

may influence the GE or VAS, such as advanced diabetes, or binge eating disorders. Furthermore, the measured tests were conducted with the gold-standard, in particular the GE test, with its well-characterized performance(29). The conducted study also has limitations. This type of study needs to be replicated in healthy weight participants and more diverse patients with obesity and obesity-related comorbidities. Furthermore, other variables such as gastric accommodation, enteroendocrine hormones, and hedonic characteristics should be considered in the measurement of satiety and satiation.

In conclusion, we report that, in real-time, simultaneous measurements, gastric emptying, and visual analog scale for appetite are correlated and both are well-validated surrogates of postprandial satiety. However, both have high coefficient of variance among our cohort of patients with obesity. Rapid GE is associated with increased appetite, which may contribute to weight gain.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data, the accuracy of the data analysis, and the decision to submit for publication.

**Data Sharing:** Data collected for the study, including individual de-identified participant data, as well as study protocol, and informed consent will be available to interested parties with publication, after signing of a data access agreement. Data may be requested by contacting Dr. Andres Acosta M.D, Ph.D., at Acosta.andres@mayo.edu.

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## RESEARCH IN CONTEXT

### What is already known about this subject?

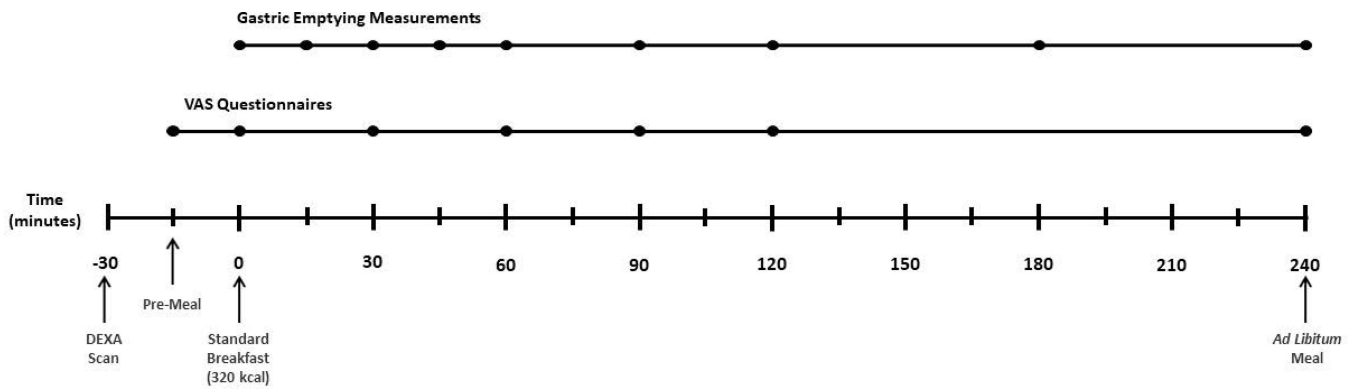
- Satiety, defined as the duration of the sensation of fullness, is usually measured by validated visual analog scales (VAS) for appetite.
- Gastric function plays a key role in food intake regulation.
- The association between gastric emptying (GE) and VAS-appetite is unknown.

### What are the new findings in your manuscript?

- Gastric emptying is associated with the sensations of appetite. However, both have a high variability.
- Both gastric emptying and VAS-appetite are associated with subsequent *ad libitum* meal intake
- Rapid gastric emptying is associated with increased appetite.

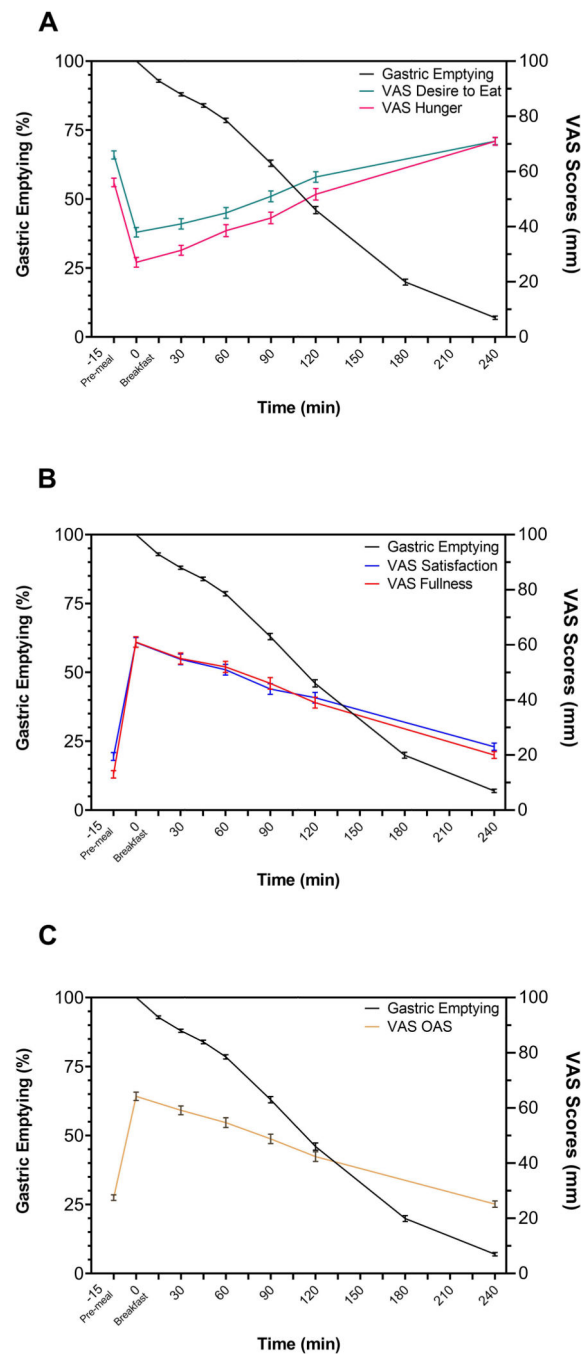
### How might your results change the direction of research or the focus of clinical practice?

- Both gastric emptying and VAS for appetite are well validated test for postprandial satiety.
- Gastric emptying may be an objective measurement for postprandial satiety.



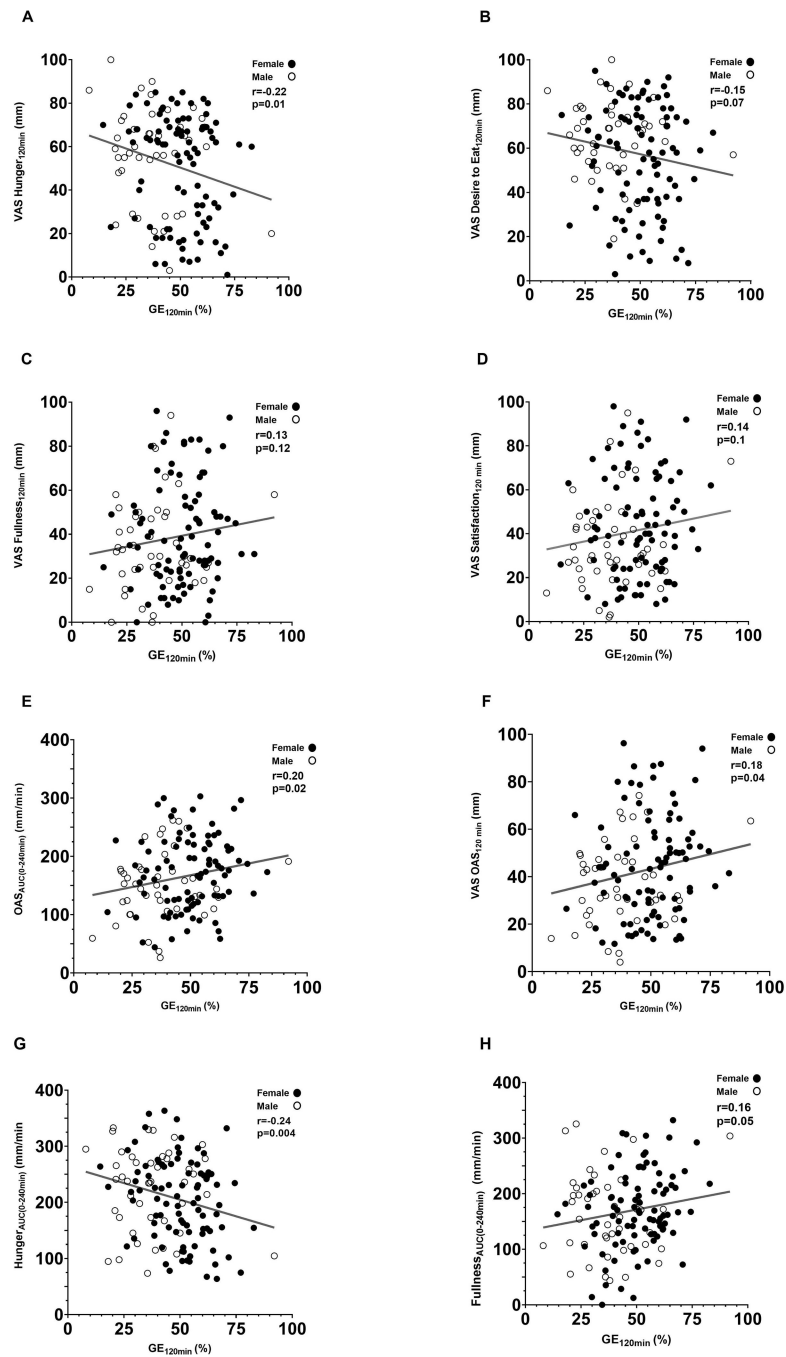
**Figure 1. Study Timeline:**

Participants presented to the Clinical Research Unit after overnight fasting. DEXA scan was performed upon patient arrival. VAS was recorded 15 minutes before a 320kcal breakfast (Pre-meal), after meal termination, and then every 30 minutes for the next 120 minutes and at 240 minutes. Gastric emptying was measured by scintigraphy with  $^{99m}\text{Tc}$ -radiolabeled eggs in the provided breakfast; images were acquired every 15 minutes for the first 60 minutes, and then at 90, 120, 180 and 240 minutes. An *ad libitum* meal was provided at 240 minutes.

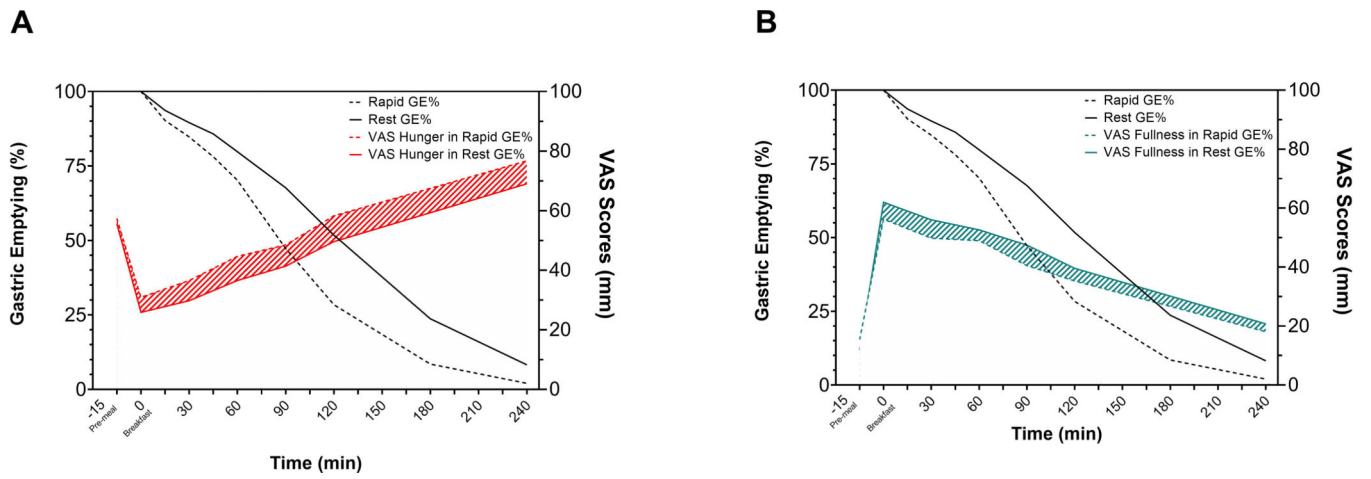


**Figure 2. GE and VAS Appetite measured simultaneously.**

A) VAS for hunger and desire to eat (mean  $\pm$  SEM) plotted against GE. After overnight fasting, hunger and desire to eat are higher, with a rapid decrease in hunger and desire to eat after the standard 320 kcal breakfast. Within the next 240 min, both sensations return to the fasting levels – increase hunger and desire to eat. B) VAS for fullness and satisfaction (mean  $\pm$  SEM) which are low during fasting, with a rapid increase after breakfast and with a gradual reduction in time. C) VAS OAS (mean  $\pm$  SEM) plotted against GE display an inverse curve where lower scores indicate higher appetite.



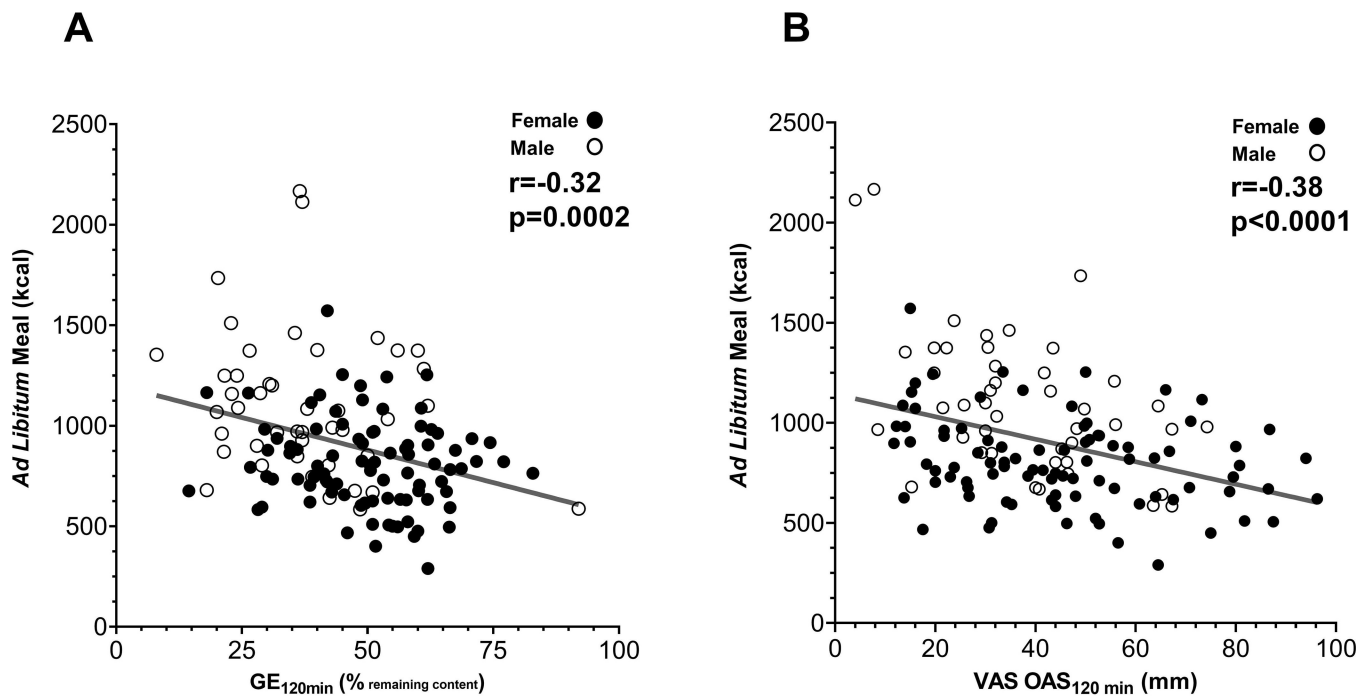
**Figure 3. Correlation between GE<sub>120min</sub> and Appetite VAS 120 min.** Percentage of meal retention at 120 minutes and its correlation with A) VAS Hunger<sub>120 min</sub>, B) VAS Desire to eat<sub>120 min</sub>, C) VAS Fullness<sub>120 min</sub>, D) VAS Satisfaction<sub>120 min</sub>, E) VAS OAS<sub>120 min</sub>, F) VAS OAS<sub>AUC(0–240 min)</sub>, G) VAS Hunger<sub>AUC(0–240 min)</sub>, and H) VAS Fullness<sub>AUC(0–240 min)</sub>. Female = dark dots; male = white dots.



**Figure 4. GE rate and VAS Appetite plotted by quartile performance.**

GE rate (mean  $\pm$  SEM) classified by quartile emptying rate performance (Rapid vs Rest) associated with A) VAS hunger and B) VAS fullness. Rapid GE is associated with higher hunger scores and lower sensation of fullness.





**Figure 5. GE<sub>120min</sub> and VAS Appetite correlation with *ad libitum* meal.**

A) GE<sub>120 min</sub>, percentage of meal retention at 120 min during the GE study, and B) VAS OAS<sub>120min</sub>, correlated negatively with total calories consumed in the *ad libitum* meal 240 minutes after breakfast. Female = dark dots; male = white dots.

**Table 1.**Demographics and Clinical Characteristics. Data shown in mean  $\pm$  SEM.

	All (n=134)	Female (n=90)	Male (n=44)	(95% CI)	<i>p</i> value
<b>Demographics</b>					
Age, y	39 $\pm$ 0.8	38.6 $\pm$ 0.9	39.8 $\pm$ 1.6	1.2 (-2.6-4.9)	0.6
Race, Caucasian (%)	126 (96) <sup>a</sup>	87 (97) <sup>b</sup>	42 (95) <sup>c</sup>	NA	0.54
Weight, kg	110.2 $\pm$ 1.9	103.9 $\pm$ 1.9	123.1 $\pm$ 3.7	19.2 (10.9 - 27.4)	<0.0001
BMI, kg/m <sup>2</sup>	37.9 $\pm$ 0.5	37.8 $\pm$ 0.6	38.2 $\pm$ 0.9	0.4(-1.8 - 2.5)	0.75
DEXA Total body fat, %	45 $\pm$ 0.8	45.3 $\pm$ 0.9	44.5 $\pm$ 1.2	-0.7 (-3.9 - 2.4)	0.63
<b>GE, %*</b>					
15 min	92.8 $\pm$ 0.5	92.9 $\pm$ 0.5	92.8 $\pm$ 0.9	-0.01 (-2.2 - 2)	0.93
30 min	88.3 $\pm$ 0.6	88.9 $\pm$ 0.6	87.2 $\pm$ 1.1	-1.7 (-4.3 - 0.9)	0.19
45 min	83.9 $\pm$ 0.7	85.2 $\pm$ 0.7	81.3 $\pm$ 1.3	-3.8 (-6.9 - -0.8)	0.02
60 min	78.5 $\pm$ 0.8	80.6 $\pm$ 0.8	74.3 $\pm$ 1.5	-6.2 (-9.7 - -2.72)	0.0007
90 min	62.6 $\pm$ 1.2	66.4 $\pm$ 1.2	55 $\pm$ 2	-11.3 (-16.1 - -6.5)	<0.0001
120 min	46 $\pm$ 1.3	50.1 $\pm$ 1.4	37.6 $\pm$ 2.3	-12.6 (-17.9 - -7.17)	<0.0001
180 min	19.9 $\pm$ 1.1	23.2 $\pm$ 1.3	13.3 $\pm$ 1.4	-9.9 (-13.8 - -6)	<0.0001
240 min	6.7 $\pm$ 0.6	8.4 $\pm$ 0.8	3.1 $\pm$ 0.5	-5.4 (-7.3 - -3.4)	<0.0001
T 1/2, min	117.3 $\pm$ 2.3	124.2 $\pm$ 2.7	103.3 $\pm$ 3.5	-20.9 (-29.8 - -12)	<.0001
<b>VAS Scores, mm</b>					
				(95% CI)	<i>p</i> value
<b>Hunger</b>					
Pre-meal	56 $\pm$ 1.6	54.4 $\pm$ 1.9	59.5 $\pm$ 2.4	5.1 (-1.3 - 11.4)	0.11
Breakfast	27 $\pm$ 1.8	25.5 $\pm$ 2.2	30.3 $\pm$ 2.8	4.9 (-2.4 - 20)	0.19
30 min	31.4 $\pm$ 1.8	28.6 $\pm$ 2.2	37.3 $\pm$ 2.9	8.7 (1.3 - 16.2)	0.02
60 min	38.5 $\pm$ 2.2	36.5 $\pm$ 2.8	42.6 $\pm$ 3.3	4.4 (-2.7 - 14.8)	0.17
90 min	43.1 $\pm$ 2.1	39.5 $\pm$ 2.6	50.4 $\pm$ 3	10.9 (2.9 - 18.9)	0.008
120 min	51.7 $\pm$ 2	49.8 $\pm$ 2.6	55.8 $\pm$ 3.4	6 (-2.5 - 14.6)	0.16
240 min	70.9 $\pm$ 1.4	70.8 $\pm$ 1.6	71.3 $\pm$ 2.7	0.5 (-5.9 - 6.9)	0.88
AUC(0-120 min), mm/min	191.4 $\pm$ 8.3	179 $\pm$ 10.4	216.8 $\pm$ 12.8	37.9 (4.9- 70.7)	0.03
AUC(0-240 min), mm/min	209.5 $\pm$ 6.4	202.8 $\pm$ 7.7	223.2 $\pm$ 11.1	20.5 (-6.6 - 47.5)	0.14
<b>Fullness</b>					
Pre-meal	12.7 $\pm$ 1.3	11.9 $\pm$ 1.5	14.3 $\pm$ 2.5	2.4 (-3.5 - 8.5)	0.42
Breakfast	60.6 $\pm$ 1.9	62.8 $\pm$ 2.3	56.1 $\pm$ 3.2	-6.6 (-14.9 - 1.7)	0.12
30 min	54.5 $\pm$ 2	56.5 $\pm$ 2.5	50.4 $\pm$ 3.2	-6.1 (-14.9 - 2.0)	0.14
60 min	51.7 $\pm$ 2	53.9 $\pm$ 2.5	47.5 $\pm$ 3.1	-6.3 (-14.4 - 1.7)	0.12
90 min	45.7 $\pm$ 2.1	48.8 $\pm$ 2.6	39.4 $\pm$ 3.2	-9.3 (-17.6 - -1.07)	0.03
120 min	38.5 $\pm$ 2	40 $\pm$ 2.5	35.5 $\pm$ 3.1	-4.5 (-12.5 - 3.6)	0.27
240 min	20 $\pm$ 1.2	20 $\pm$ 1.4	20.31 $\pm$ 2.2	0.3 (-5 - 5.7)	0.90
AUC(0-120 min), mm/min	251.8 $\pm$ 8.6	262.6 $\pm$ 10.6	229.8 $\pm$ 14.3	-32.8 (-68.3 - 2.8)	0.07

	All (n=134)	Female (n=90)	Male (n=44)	(95% CI)	<i>p value</i>
AUC(0–240 min), mm/min	168.3 ± 6.2	171 ± 7.4	163 ± 11.1	–7.9 (–34.6 – 18.7)	0.55
<b>OAS</b>					
120 min	42.4 ± 1.8	44.7 ± 2.2	37.5 ± 2.5	–7.2 (–14.1 – –0.35)	0.04
240 min	25.2 ± 1.1	22.5 ± 1.3	24.4 ± 2	–1.2 (–6.1 – 3.8)	0.64
AUC(0–120 min), mm/min	270.4 ± 7.5	282.7 ± 9.3	245.1 ± 11.7	–37.5 (–67.3 – –7.8)	0.01
AUC(0–240 min), mm/min	164.4 ± 5.3	171.5 ± 6.6	149.72 ± 8.6	–21.8 (–43.4 – –0.21)	0.05
<b>Satiation test</b>					
<i>Ad libitum</i> meal, kcal	905.1 ± 26.5	806.9 ± 23.5	1106 ± 53.3	299 (182 – 415.8)	<0.0001
Protein, %	22.7 ± 0.2	22.8 ± 0.2	22.5 ± 0.3	–0.4 (–1.2 – 0.5)	0.40
Fat, %	20.6 ± 0.2	20.4 ± 0.2	20.9 ± 0.3	0.4 (–0.3 – 1.2)	0.27
Carbohydrates, %	56.7 ± 0.2	56.7 ± 0.2	56.6 ± 0.4	–0.1 (–1.2 – 1.02)	0.86

Abbreviations: , mean difference between gender groups; CI, confidence interval; BMI, body mass index; GE, gastric emptying; VAS, visual analog scale; AUC, area under the curve; OAS, overall appetite score.

\* : % of meal retention at each time point

a) 3% Asian, 1% African American

b) 2% Asian, 1% African American

c) 5% Asian

**Table 2.**

Gastric Emptying and VAS appetite test in rapid GE quartile group compared to rest (other 3 quartiles) group. Data shown in mean  $\pm$  SEM.

	<b>Rapid (n=33)</b>	<b>Rest (n=101)</b>	<i>p value</i>	
<b>GE</b>				
GE T 1/2, min	88.6 $\pm$ 2.3	126.7 $\pm$ 2.3	<.0001	
<b>VAS Scores, mm</b>				
<b>Hunger</b>			<b>(95% CI)</b>	<i>p value</i>
120 min	58.3 $\pm$ 3.8	49.6 $\pm$ 2.4	-8.7 (-17.8 - 0.5)	0.07
240 min	76.7 $\pm$ 2.1	69 $\pm$ 1.7	-7.7 (-13.2 - -2.1)	0.008
AUC(0-240 min), mm/min	233.2 $\pm$ 11.9	201.7 $\pm$ 7.4	-32 (-59.7 - -3.2)	0.03
<b>Fullness</b>				
120 min	35.3 $\pm$ 3.8	39.6 $\pm$ 2.3	4.3 (-4.7 - 13.3)	0.34
240 min	18.1 $\pm$ 2.1	20.8 $\pm$ 1.4	2.7 (-2.6 - 7.9)	0.31
AUC(0-240 min), mm/min	154.9 $\pm$ 13.2	172.8 $\pm$ 6.9	18 (-12.1 - 47.9)	0.21
<b>OAS</b>				
120 min	39 $\pm$ 3.5	43.5 $\pm$ 2	16.9 (-3.7 - 12.7)	0.28
240 min	22.6 $\pm$ 2.1	26 $\pm$ 1.3	3.4 (-1.6 - 8.5)	0.18
AUC(0-240 min), mm/min	151.7 $\pm$ 10.7	168.5 $\pm$ 6.1	4.5 (-7.8 - 41.6)	0.17

Abbreviations: , mean difference between rapid and rest groups; CI, confidence interval; GE, gastric emptying; VAS, visual analog scale; AUC, area under the curve; OAS, overall appetite score.