Assessment of antral grinding of a model solid meal with echo-planar imaging

LUCA MARCIANI,1 PENNY A. GOWLAND,1 ANNETTE FILLERY-TRAVIS,2 PRE蒂MA MANOJ,2 JEFF WRIGHT,3 ANDREW SMITH,2 PAUL YOUNG,1 RACHEL MOORE,1 AND ROBIN C. SPILLER4

1Magnetic Resonance Center, School of Physics and Astronomy, Nottingham NG7 2RD; 2Institute of Food Research, Colney, Norwich NR4 7UA; and 3Surgery and 4Division of Gastroenterology, Queen’s Medical Center, University Hospital, Nottingham NG7 2UH, United Kingdom

Received 25 April 2000; accepted in final form 1 December 2000

Marciani, Luca, Penny A. Gowlan, Annette Fillery-Travis, Pretima Manoj, Jeff Wright, Andrew Smith, Paul Young, Rachel Moore, and Robin C. Spiller. Assessment of antral grinding of a model solid meal with echo-planar imaging. Am J Physiol Gastrointest Liver Physiol 280: G844–G849, 2001.—Mathematical modeling of how physical factors alter gastric emptying is limited by lack of precise measures of the forces exerted on gastric contents. We have produced agar gel beads (diameter 1.27 cm) with a range of fracture strengths (0.15–0.90 N) and assessed their break-down by measuring their half-residence time (RT1/2) using magnetic resonance imaging. Beads were ingested either with a high (HV)- or low (LV)-viscosity liquid nutrient meal. With the LV meal, RT1/2 was similar for bead strengths ranging from 0.15 to 0.65 N but increased from 22 ± 2 min (bead strength <0.65 N) to 65 ± 12 min for bead strengths >0.65 N. With the HV meal, emptying of the harder beads was accelerated. The sense of fullness after ingesting the LV meal correlated linearly (correlation coefficient = 0.99) with gastric volume and was independently increased by the harder beads, which were associated with an increased antral diameter. We conclude that the maximum force exerted by the gastric antrum is close to 0.65 N and that gastric sieving is impaired by HV meals.
against residence time would allow assessment of the maximum force exerted. Because increased meal viscosity is known to facilitate the emptying of indigestible particles (22, 23, 27), we were interested in how this altered the antral handling of the beads. Our previous work (19) indicated that varying meal viscosity by 1,000-fold has minimal effect on the emptying of a liquid meal, so we hypothesized that the stomach would react to increasing viscosity by increasing the force of contraction and thus increasing the fracture strength above which gastric emptying of beads was delayed. Our studies (19) and those of Krotiewsky (15) also indicate that viscosity has a major impact on satiety, though whether this is direct or indirect via impaired absorption and subsequent stimulation of intestinal receptors (8, 24) probably depends on the meal type. We hypothesized, therefore, that increasing viscosity would increase satiety.

MATERIALS AND METHODS

Test meals. Spherical (1.27-cm diameter) agar gel beads of seven linearly increasing fracture forces (from 0.15 to 0.90 N) were produced by boiling food-grade agar gel (Gelidium amansii; Hispanagar, Burgos, Spain) in an autoclave at 121°C for 1 h. Trace amounts of barium sulfate (E-Z-HD powder; E-Z-EM) and ferrous fumarate (Fersamal syrup; Forley, Dublin, Ireland) were added to increase the density and MRI contrast, respectively. The liquid hot gel was injected into an aluminum mold, which was then left to cool down slowly overnight. The rheological behavior of the agar gel was assessed using a Bohlin VOR rheometer (Cirencester, UK) with the cone and plate geometry. The gelation properties, from liquid solution to gel, were measured for six different agar gel concentrations between 0.75% and 3% (wt/wt) to determine whether the trace amounts of barium sulfate and ferrous fumarate would modify the gel strength properties. Agar gel bead compression tests were then carried out using a TA.XT2 texture analyzer (Stable MicroSystem) with a 5-kg load cell. The force-displacement data were recorded for eight beads for each of six different agar gel concentrations between 0.75% and 3% (wt/wt). The maximum force corresponding to failure of the bead and the initial slope of the force-displacement curve, which is proportional to the stiffness of the bead, were measured from the data. Locust bean gum (LBG, Ceratonia siliqua, food grade; Lucas Meyer Colloids, Chester, UK) test meals of either low (LV; 0.06 Pa·s) or high (HV; 29.5 Pa·s) viscosity were prepared by adding appropriate amounts of gum powder to 500 ml of boiling hot water. The solutions were blended using a food mixer and were then kept at 90°C for 1 h before being allowed to cool down slowly. The LV LBG meal was similar to water, whereas the HV meal was just barely pourable. Both LV and HV meals contained carbohydrates and emulsified olive oil as nutrients (1,350 kJ) and had an osmolality of 200 mosmol/kgH2O. Banana flavoring was also added to improve palatability.

Subjects. Sixteen healthy volunteers (8 male and 8 female; age, 30 ± 5 yr; body mass index, 22 ± 0.5 kg/m2), who had no history of gastrointestinal disorders and were taking no regular medication, attended seven separate experimental morning sessions (>1 day and <1 wk apart), having fasted overnight on each occasion. Volunteers were divided into two groups of eight subjects (4 male and 4 female in each group).

One group received the LV meal and the other the HV meal. On each occasion, subjects ingested without chewing 15 agar gel beads from one of the 7 strength batches, together with 500 ml of the appropriate meal. The time when meal ingestion started was defined as time 0. Subjects were blinded to the strength of the beads, which were given in random order on the different experiment days to avoid order effects. Subjects were asked to hold their breath before each image acquisition to minimize diaphragmatic displacement. Between scanning, they were asked to sit upright on the scanning bed, lying down only for the time necessary to acquire the images. This protocol was approved by the University Medical School Ethics Committee, and volunteers gave informed written consent before experiments.

EPI. Single-shot EPI (14, 17) images were acquired on a 0.5-T purpose-built whole body EPI scanner equipped with actively shielded gradients and a 50-cm-diameter birdcage coil. The in-plane resolution was 3.5 × 2.5 mm, and the slice thickness was 1 cm. Each image was acquired in 130 ms using a 128 × 128 matrix with an effective echo time of 40 ms. After ingestion of the beads and the LBG meal, a transverse, rapid, multislice set of images of the subject was acquired from the heart to the kidneys to determine the position of the gastric lumen (total scan time 4 s). Similar multislice data sets were then acquired every 15 min for 1.5 h. One rapid multislice set (a block of 5 contiguous slices scanned every 3 s; total scan time 4 min) was obtained across the antrum to assess antral motility. The number of intact beads remaining in the stomach at each time point was calculated. For each experiment, a curve of the number of intact beads remaining in the stomach was plotted against time and the half-residence time (RT1/2) of intact beads in the stomach was averaged for each bead strength. The time needed to empty one-half of the initial total gastric volume, the half-emptying time (t1/2) (5), was calculated from the volume-time curve for each subject and meal and averaged per bead strength. We observed that the beads tended to accumulate in the dependent antral region. Antral distension has been related to early satiety in patients with functional dyspepsia (29), and Marzio et al. (21) indicated that the antrum is sensitive to distension. We therefore measured maximum antral diameters on coronal view reconstructions of the multislice sets for the LV meal and related this to satiety.

Satiety. The subjective feelings of satiety (12) of the volunteers were assessed using a self-report scale technique. Before meal ingestion and every 15 min afterward, volunteers were asked to give numbers between 1 and 10 to indicate 1) how full they felt (1 = “not full” and 10 = “extremely full”), 2) how hungry they were (1 = “not hungry” and 10 = “extremely hungry”), and 3) how much food they would eat (1 = “nothing” and 10 = “an enormous meal”) at that given time. The scores were then averaged between subjects for each bead strength and meal.

Data analysis. EPI images were analyzed by one operator blinded to the experimental conditions. The gastric volume (every 15 min) and motility data (1) were analyzed as described previously (19, 20). Subsequently, statistical analysis was performed using the multivariate ANOVA test for repeated measures on SPSS software (Chicago, IL). Results are expressed as means ± SE.

RESULTS

Test meals. We measured the fracture forces for agar gel bead (shown in Fig. 1A) concentrations between 0.75% and 3%. They ranged from 0.15 and 0.90 N

EPI. Single-shot EPI (14, 17) images were acquired on a 0.5-T purpose-built whole body EPI scanner equipped with actively shielded gradients and a 50-cm-diameter birdcage coil. The in-plane resolution was 3.5 × 2.5 mm, and the slice thickness was 1 cm. Each image was acquired in 130 ms using a 128 × 128 matrix with an effective echo time of 40 ms. After ingestion of the beads and the LBG meal, a transverse, rapid, multislice set of images of the subject was acquired from the heart to the kidneys to determine the position of the gastric lumen (total scan time 4 s). Similar multislice data sets were then acquired every 15 min for 1.5 h. One rapid multislice set (a block of 5 contiguous slices scanned every 3 s; total scan time 4 min) was obtained across the antrum to assess antral motility. The number of intact beads remaining in the stomach at each time point was calculated. For each experiment, a curve of the number of intact beads remaining in the stomach was plotted against time and the half-residence time (RT1/2) of intact beads in the stomach was averaged for each bead strength. The time needed to empty one-half of the initial total gastric volume, the half-emptying time (t1/2) (5), was calculated from the volume-time curve for each subject and meal and averaged per bead strength. We observed that the beads tended to accumulate in the dependent antral region. Antral distension has been related to early satiety in patients with functional dyspepsia (29), and Marzio et al. (21) indicated that the antrum is sensitive to distension. We therefore measured maximum antral diameters on coronal view reconstructions of the multislice sets for the LV meal and related this to satiety.

Satiety. The subjective feelings of satiety (12) of the volunteers were assessed using a self-report scale technique. Before meal ingestion and every 15 min afterward, volunteers were asked to give numbers between 1 and 10 to indicate 1) how full they felt (1 = “not full” and 10 = “extremely full”), 2) how hungry they were (1 = “not hungry” and 10 = “extremely hungry”), and 3) how much food they would eat (1 = “nothing” and 10 = “an enormous meal”) at that given time. The scores were then averaged between subjects for each bead strength and meal.

Data analysis. EPI images were analyzed by one operator blinded to the experimental conditions. The gastric volume (every 15 min) and motility data (1) were analyzed as described previously (19, 20). Subsequently, statistical analysis was performed using the multivariate ANOVA test for repeated measures on SPSS software (Chicago, IL). Results are expressed as means ± SE.

RESULTS

Test meals. We measured the fracture forces for agar gel bead (shown in Fig. 1A) concentrations between 0.75% and 3%. They ranged from 0.15 and 0.90 N
(average SE 8%), and a simple natural logarithmic (ln) relationship (Fig. 1B) was found between the bead fracture threshold (F) and agar gel concentration (C) $F = 0.5419 \ln(C) + 0.3081$, correlation coefficient ($r^2 = 0.95$). We also measured the variation of the slope ($S$) of the compression curve (Fig. 1C), and an exponential relationship with agar concentration (C) was found ($S = 0.011e^{1.011C}$, $r^2 = 0.96$). The calibration curve of the fracture force (Fig. 1B) was used to determine the seven agar gel concentrations required to produce seven batches of beads with linearly increasing fracture force between 0.15 and 0.90 N. Both LV and HV meals were well tolerated by subjects and ingested with the 15 beads within the requested 10 min. With the EPI sequence, the meals inside the gastric lumen were found to provide good contrast, which enabled us to discriminate the stomach contents from the surrounding tissues. Furthermore, the agar gel beads were clearly distinguishable against the test meal; in most cases, the majority of beads accumulated in the antral area (Fig. 2A).

Emptying of beads. The agar gel beads tended to fracture in numerous smaller irregular fragments as shown in Fig. 1A. These were readily distinguishable from the much larger, smooth intact beads. The in-plane resolution of the images was excellent, allowing discrimination of fragments a few millimeters in size.

On four occasions, an intact hard bead (breaking strength >0.65N) was detected in the upper duodenum (Fig. 2C). The average decline in the number of intact beads in the stomach with time was exponential in shape for both meals ($r^2 = 0.79$). With the LV meal, RT$_{1/2}$ of intact beads in the gastric lumen doubled when the fracture threshold of the beads was >0.65 N (Fig. 3). The difference in RT$_{1/2}$ of the 0.78- and 0.9-N beads vs. each one of the lower five bead strengths was highly significant ($P < 0.002$) with the LV meal. With the HV meal instead, RT$_{1/2}$ increased by 40% when the breakdown force of the beads was >0.53 N (Fig. 3), but this difference in RT$_{1/2}$ was not significant ($P < 0.45$). Increasing meal viscosity decreased the overall RT$_{1/2}$ ($n = 56$, averaged for all bead strengths) from 37 ± 3 min for the LV meal to 26 ± 2 min for the HV meal ($P < 0.03$). Fragments of soft beads were often seen in the images (Fig. 2B).

Meal emptying. The average emptying curve for the total gastric volume (liquid and solid) was exponential...
in shape ($r^2 = 0.99$ for both meals). Figure 4 shows $t_{1/2}$ for the fracture forces for all beads and both meals. An overall effect of increasing bead strength to delay emptying of the total gastric contents for both the LV ($P < 0.03$) and HV meals ($P < 0.01$) was found. Increasing meal viscosity delayed $t_{1/2}$ ($n = 56$, averaged for all bead strengths) from 37 ± 3 min for the LV meal to 48 ± 2 min for the HV meal ($P < 0.02$).

**Antral motility.** The effect of bead strength or meal viscosity on the average antral contraction frequency or propagation speed was not significant ($P, 0.1–0.7$). Average values ($n = 56$, averaged for all bead strengths) were 2.98 ± 0.03 contractions/min and 1.57 ± 0.04 mm/s for the LV meal and 2.92 ± 0.03 contractions/min and 1.55 ± 0.03 mm/s for the HV meal.

**Satiety.** Increasing bead strength increased the satiety scores for fullness from 4.4 ± 0.5 to 5.6 ± 0.5 for the LV meal ($P < 0.0001$) and the HV meal ($P < 0.03$). No other differences were significant ($P < 0.1–1$).

**Satiety vs. gastric volumes.** Figure 5 shows the fullness scores plotted against the total gastric volume at corresponding time points for the fracture force for the lowest (0.15 N) and highest beads (0.90 N) and for both meals. Interestingly, a linear relationship ($r^2 = 0.99$) between fullness and gastric volume for the beads with the lowest fracture force with the LV meal was found. The satiety-volume curve for the beads with the highest fracture force with the LV meal deviated from linearity, showing a higher sense of fullness for a given gastric volume compared with the low fracture force beads (Fig. 5A). The respective satiety-volume curves for the HV meal are also nonlinear, with little differ-
ence between the two (Fig. 5B). Appetite and hunger decreased with increasing gastric volumes, but no significant differences were found.

**Antral diameters.** The maximum antral diameters were measured for the LV meal only, to investigate further possible factors that could explain the observed differences in the curve of fullness vs. total gastric volumes for that meal. The maximum antral diameter for the lowest (0.15 N) bead strength (4.7 ± 0.3 cm) was significantly smaller than the one for the highest (0.90 N) bead strength (6.1 ± 0.2 cm) (P < 0.01).

**DISCUSSION**

Until recently, little was known about the forces exerted by the stomach on meal components. By using solid beads of different strengths and an LV liquid meal, we were able to define a threshold of 0.65 N above which beads emptied significantly more slowly, confirming our first hypothesis. Below that value we observed bead fragments in the stomach. Therefore it was possible to infer that the force exerted by the antral walls in grinding food is between 0.53 and 0.78 N. Previous attempts (3) to measure axial forces used a 1.8-cm balloon, which was mounted on a tube and fixed a few centimeters from the antrum. The cumulative forces recorded averaged 6 and 22 N for the emptying of a liquid or solid meal, respectively (30). The average force per contraction averaged 0.2 N (30), lower than that measured in our study, but the technique used is not directly comparable with our technique. However, the range of breakdown forces measured in our study are consistent with the observation of Vasallo et al. (30) that antral axial forces are mostly <1 N. It is important to note that the balloon used by Vasallo et al. (30) could not move freely toward the pylorus, where the near synchronous “systolic” contraction of the distal antrum exerts the maximal force and solids appear to break up (2). This might explain why we measured higher maximal forces.

When meal viscosity was increased, we observed that even the harder beads were emptying faster and the step up in RT1/2 could not be reliably observed, so our second hypothesis could not be substantiated. An improved knowledge of this behavior would allow mathematical modeling of the physical processes involved in gastric emptying of a complex model meal.

Gastric sieving, the process whereby the liquid component of a liquid solid meal leaves the stomach ahead of the solid component, has been recognized for many years (13). The antrum and pylorus appear critical for this process, because antrectomy markedly increases the amount of larger food particles entering the small bowel (25). Cineradiology (4) shows that solids are propelled toward the pylorus by antral contractions and those that exceed a threshold of ~2-mm diameter are usually retropropelled back into the stomach by pyloric contractions. This process also occurs with fatty liquid meals and appears to be a fundamental factor regulating gastric emptying and encouraging the trituration and emulsification of gastric chyme (1). Direct imaging of solid and liquid meals using MRI and ultrasound has shown that the solids tend to lie dependently in the stomach, allowing fluid to “decant” over them (2). Of course, in the normal process of digestion the two phases mix (31), and this liquid phase becomes more viscous. The HV meal did accelerate gastric emptying of beads, though the overall total gastric emptying (beads plus meal) was actually slightly slower. This suggests that the main effect of increasing viscosity was to prevent the sedimentation of the beads and enhance the efficiency of antral grinding, facilitating their rapid breakdown and emptying. Beads suspended in the axial flow will be exposed to the maximum shear forces while being propelled toward the pylorus.

In these studies, we confirmed the previously (18) observed linear relationship between fullness and gastric volume with an LV test meal. Earlier studies (9) have clearly shown that eating a whole apple caused much greater satiety than consuming the same amount of apple pureed. Although our hypothesized effect of increased meal viscosity increasing satiety was not confirmed, we did find that harder beads produced greater satiety. Although this could in part be due to the delay in gastric emptying, we found a leftward shift of the fullness vs. volume curve. This indicates that the hardness of the beads had an additional effect independent of the rate of gastric emptying. One may hypothesize that the stomach can somehow detect failure of the beads to break up and hence signal increased satiety. This may be related to either an increase in antral forces and hence wall tension or the observed increase in maximum antral diameters with the hard beads, which possibly stimulate stretch receptors in the antrum. The antrum, being inherently smaller, is generally more sensitive to stretch than the proximal stomach in both functional dyspepsia and healthy volunteers so that for any given diameter the sensation of fullness is greater for antral than proximal gastric distension (21). Interestingly, with increased viscosity this ability for sense of satiety to vary with bead strength seems to disappear. This would be compatible with the evidence that increased viscosity prevents sedimentation of particles, speeds their emptying (27), and so may prevent antral distension.

In summary, we have shown using this novel technique that beads of a breaking strength >0.65 N show a delayed exit from the stomach. Softer beads are rapidly broken and empty at the same rate as a liquid meal. Unyielding objects in the stomach increase satiety by an unknown mechanism that involves the antrum and warrants further study.

We gratefully acknowledge Dr. P. Boulby for helpful discussions and Dr. Ron Coxon and Paul Clark for technical assistance. This study was supported by the Biotechnology and Biological Sciences Research Council (Swindon, UK).

Present address of P. Manoj: Dupont Cereals Innovation Center, Cambridge CB1 2UJ, United Kingdom.
REFERENCES


