*Am J Physiol Gastrointest Liver Physiol*
281: G1214–G1220, 2001.

# Pressure-geometry relationship in the antroduodenal region in humans

HENRYK FAAS,[1] GEOFFREY S. HEBBARD,[2] CHRISTINE FEINLE,[3] PATRIK KUNZ,[1]
JAMES G. BRASSEUR,[4] K. INDIRESHKUMAR,[4] JOHN DENT,[2] PETER BOESIGER,[1]
MIRIAM THUMSHIRN,[3] MICHAEL FRIED,[3] AND WERNER SCHWIZER[3]
[1]*Biophysics Group, Institute of Biomedical Engineering, University of Zurich and Eidgenössische Technische Hochschule Zurich, 8091 Zurich, Switzerland;* [2]*Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia;* [3]*Department of Gastroenterology, University Hospital Zurich, 8091 Zurich, Switzerland; and* [4]*Department of Mechanical Engineering, Pennsylvania State University, University Park, Pennsylvania 16802*

Received 29 November 2000; accepted in final form 13 July 2001

**Faas, Henryk, Geoffrey S. Hebbard, Christine Feinle, Patrik Kunz, James G. Brasseur, K. Indireshkumar, John Dent, Peter Boesiger, Miriam Thumshirn, Michael Fried, and Werner Schwizer.** Pressure-geometry relationship in the antroduodenal region in humans. *Am J Physiol Gastrointest Liver Physiol* 281: G1214–G1220, 2001.—Understanding of the control mechanisms underlying gastric motor function is still limited. The aim of the present study was to evaluate antral pressure-geometry relationships during gastric emptying slowed by intraduodenal nutrient infusion and enhanced by erythromycin. In seven healthy subjects, antral contractile activity was assessed by combined dynamic magnetic resonance imaging and antroduodenal high-resolution manometry. After intragastric administration of a 20% glucose solution (750 ml), gastric motility and emptying were recorded during intraduodenal nutrient infusion alone and, subsequently, combined with intravenous erythromycin. Before erythromycin, contraction waves were antegrade (propagation speed: 2.7 ± 1.7 mm/s; lumen occlusion: 47 ± 14%). Eighty-two percent (51/62) of contraction waves were detected manometrically. Fifty-four percent of contractile events (254/473) were associated with a detectable pressure event. Pressure and the degree of lumen occlusion were only weakly correlated ($r^2 = 0.02$; $P = 0.026$). After erythromycin, episodes of strong antroduodenal contractions were observed. In conclusion, antral contractions alone do not reliably predict gastric emptying. Erythromycin induces strong antroduodenal contractions not necessarily associated with fast emptying. Finally, manometry reliably detects ~80% of contraction waves, but conclusions from manometry regarding actual contractile activity must be made with care.

magnetic resonance imaging; manometry; gastric motility; erythromycin

THE DEFICIENCIES in our current understanding of the mechanics of antropyloroduodenal motor function contributing to gastric emptying (GE) in humans can be attributed largely to technical difficulties in the simultaneous assessment of GE, gastric wall motion, and intraluminal pressures. The majority of studies so far have relied exclusively on the measurement of one of these variables. Gastrointestinal motility is most commonly assessed by luminal manometry. It has good temporal resolution, but the relationship between pressure patterns and actual contractile patterns is not entirely clear. To gain insight into this relationship, a few studies have been performed to complement manometric information by techniques providing information on wall motion (4, 11, 17, 18). As the organization of the mechanical factors that determine GE is complex, the ability to simultaneously record gastric wall motion and intraluminal pressures on a second-to-second basis may add important information to that gained from measurement of pressure alone (8, 12).

Therefore, the aim of the present study was to evaluate the pressure-geometry relationships of the antropyloroduodenal region during GE slowed by intraduodenal nutrient infusion by a combination of dynamic three-dimensional (3D) magnetic resonance (MR) imaging (MRI) with simultaneous high-resolution manometry. We further aimed to investigate the effects of the motilin agonist erythromycin on the mechanics of the distal stomach.

## METHODS

### Subjects

Seven healthy subjects (5 men, 2 women) aged 23–45 yr participated in the study. All subjects gave written informed consent, and the study protocol was approved by the Ethics Committee of the Department of Internal Medicine at the University Hospital Zurich.

### Experimental Protocol

Figure 1*A* shows the experimental protocol. Subjects reported to the laboratory after an overnight fast. The manometric assembly, which had a chain of 19 recording sideholes

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Address for reprint requests and other correspondence: W. Schwizer, Dept. of Internal Medicine, Gastroenterology, University Hospital Zurich, 8091 Zurich, Switzerland (E-mail: gasschwi@usz.unizh.ch).

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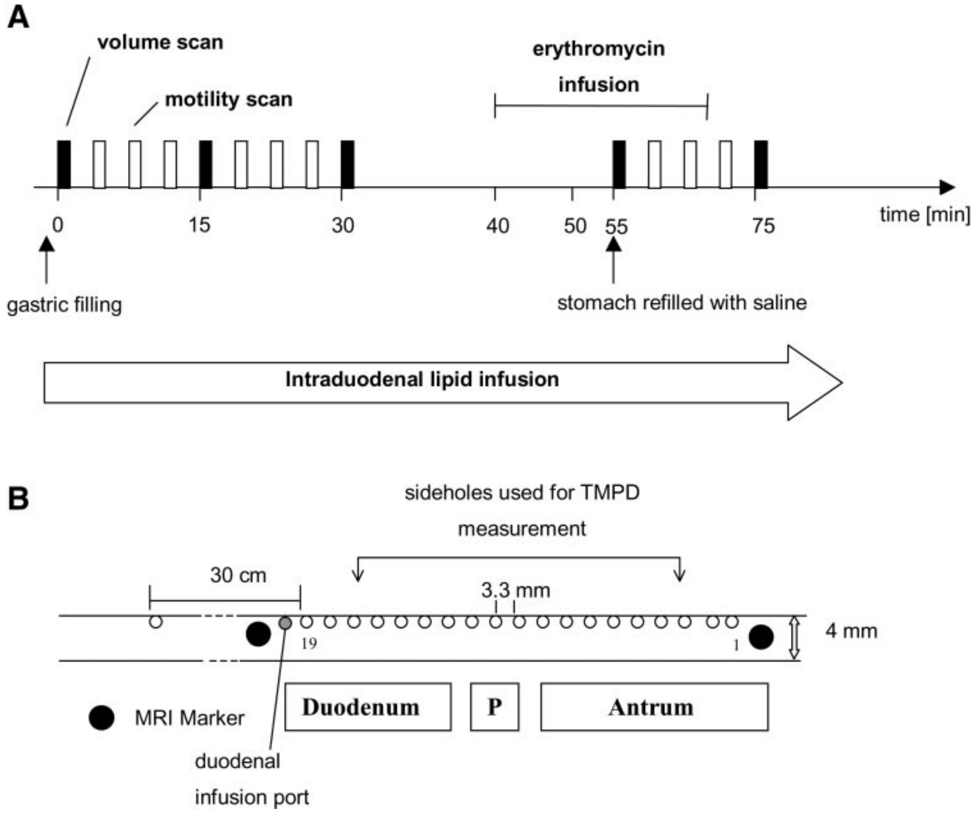

Fig. 1. *A*: study protocol. A series of 4 magnetic resonance (MR) imaging (MRI) scans, a "volume scan" (to measure intragastric liquid volume) and 3 "motility scans" (to assess antroduodenal wall motion), were performed 3 times. Before the 3rd series, erythromycin (200 mg) was administered intravenously. Pressures were recorded continuously throughout the study, and an intraduodenal nutrient infusion was maintained at 2.1 kcal/min. *B*: manometric assembly shows the arrangement of the perfused sideholes and the markers, which indicated the zone of pressure recording sideholes of the assembly in the MR images. Transmucosal potential difference (TMPD) recording was used to allow correct positioning of the catheter across the gastroduodenal junction. P, pylorus.

spaced at 3.3-mm intervals (Fig. 1*B*), was inserted through an anesthetized nostril and positioned across the pylorus using previously validated transmucosal potential difference (TMPD) criteria. The position of the catheter was controlled visually by two stainless steel MR markers on both sides of the pressure-sensitive zone. A second tube (inner diameter 1.5 mm; outer diameter 2.5 mm) that ran alongside the manometric assembly ended in the stomach and was used for intragastric infusions. An intravenous catheter for the infusion of placebo (saline solution) or erythromycin (Erythrocine; Abbott, Baar, Switzerland) was inserted into the antecubital fossa. Fifteen minutes after phase III of the interdigestive migrating motor complex had passed the most distal duodenal recording channel, an intraduodenal nutrient infusion [equal vols of 25% dextrose and a 10% lipid emulsion (1.1 kcal/ml, Intralipid; Kabi-Vitrum, Stockholm, Sweden)] was started at a rate of 2 ml/min (2.1 kcal/min). This rate was maintained throughout the study. The subject was placed in the MR scanner supine at 30° toward the left lateral position to ensure filling of the antrum. Isotonic saline solution (750 ml), marked with 600 μM gadolinium tetraazacyclododecane tetraacetic acid (Dotarem; Laboratoire Guerbet, Aulnay-sous-Bois, France) as a paramagnetic MRI contrast agent (16), was infused intragastrically over 4 min through the gastric tube. Antropyloroduodenal pressures were recorded throughout the study with transducer drift being assessed and corrected every 15 min.

*Part 1.* Immediately after the intragastric saline infusion, an MR scan was performed to measure the intragastric liquid volume ("volume scan"; see *Magnetic Resonance Imaging*). This was followed by three dynamic MR scans of 90-s duration each to assess gastric motility ("motility scan"; see *Magnetic Resonance Imaging*). This basic sequence was repeated twice at 15-min intervals (total 30 min).

*Part 2.* Starting at $t = 40$ min, 200 mg of erythromycin were given as an intravenous infusion over 20 min. At $t = 45$ min another 750 ml of isotonic saline solution were infused, and at $t = 50$ min another volume scan and three motility scans were performed for 15 min. The observation time was limited to 15 min because we found in pilot studies that the gastric lumen was almost empty within 15 min after intravenous infusion of erythromycin.

### *MRI*

All studies were performed in a 1.5-T whole body imager (Philips Gyroscan ACS-NT, Best, The Netherlands). Two different types of scans were used: *1*) a scan to determine the amount of liquid in the gastric lumen (volume scan) and *2*) a scan to assess gastric wall motion in three dimensions (motility scan).

*Volume scan to assess GE.* Intragastric liquid volume was measured using a Turbo Spinecho scan (transverse slice orientation; echo time = 12 ms; repetition time = 576 ms; flip angle: 90°) with 24 contiguous slices acquired over 60 s. Spatial resolution was $1.5 \times 1.5 \times 7.5$ mm$^3$ (matrix size: $256 \times 256$ pixels; field of view: 380 mm). To avoid motion artifacts, the scan was divided into four measurement periods of 15 s each and the subjects were asked to hold their breath in expiration during the length of these measurements. GE was quantified by calculating gastric volume. In all 24 slices of a volume scan, the contour of gastric content was outlined semiautomatically. These areas were multiplied by the slice thickness and added to obtain the intragastric volume (15).

*Motility scan.* A dynamic scan was designed to assess 3D wall motion in the antropyloroduodenal area and to track the position of the manometric assembly markers (see *Manomet-*

*ric Technique*) to determine the exact position relative to the pylorus and antrum. Over 90 s, seven slices were acquired each second using a multislice echo planar imaging (EPI) sequence (coronal slice orientation; EPI factor 5; echo time = 5 ms; repetition time = 81 ms; flip angle: 20°; matrix size: 128 × 128 pixels; field of view: 384 mm; in-plane resolution: 3 × 3 mm; slice thickness: 7 mm). The scan was triggered by a signal from the computer that acquired the manometric data to synchronize MRI and manometric data.

### *Manometric Technique*

A water perfusion manometry system with optimized electronics (transducer drift $< 0.1$ mmHg/15 min; Sedia, Fribourg, Switzerland) was used to record pressures along a catheter with 21 ports (lumen diameter: 0.4 mm; outer diameter: 4 mm), 19 of which were used for pressure measurement in this study and 1 for intraduodenal nutrient infusion, as illustrated in Fig. 2 (0.4-mm inner diameter recording channels; Dentsleeve, Parkside, Australia). The system had a pressure response rate of $\geq$150 mmHg/s on sidehole occlusion. The catheter was preflushed with $CO_2$ to eliminate air bubbles, and water perfusion was limited to 0.08 ml/min. To obtain high spatial resolution throughout the antropyloroduodenal region, the 19 pressure recording ports were spaced 3.3 mm apart along a 6-cm segment of the assembly. The third and seventeenth sideholes were perfused with normal saline from separate reservoirs; and TMPD was monitored concurrently with manometry to aid the positioning of the catheter across the pylorus. Manometric data were recorded at 8 samples/s. Transducer drift was regularly corrected over the study period with an underwater reference, and measurement uncertainty was minimized to within 0.5 mmHg. All pressures were expressed relative to a baseline pressure defined as the fifth percentile of the pressure values in the duodenum (19th manometric channel) during *part 1* of the study. Recordings were analyzed only when the TMPD readings indicated that the assembly was correctly positioned across the pylorus.

### *Data Analysis*

*Terminology.* The term "propagating wave" is used in this article to imply propagation between at least two points of observation. The general term "motility" refers to motor function as measured by either manometry or MRI. Individual wall indentations are called contractile events (contractions). A spatial progression of contractile events in time is defined as a propagating contraction wave. Pressure increases of at least 5 mmHg above baseline [see *Pressure waves (manometry)*] in a single manometric channel are defined as pressure events. Pressure events showing a progression in time over at least two manometric channels are called propagating pressure waves.

*Pressure waves (manometry).* A computer program was developed to detect antral pressure events and waves (manometric data displayed as contour plots). The area under the curve (AUC) was defined in each antral channel as the area under the pressure vs. time curve during pressure events. The AUC was calculated relative to antral baseline and scaled to 15 min for each study period. The channel with maximum AUC was used to distinguish levels of antral pressure activity between subjects. Pressures recorded from all channels proximal to the pyloric channels were used to determine mean antral pressure. All channels distal to the pylorus yielded the mean duodenal pressure, and the pyloric

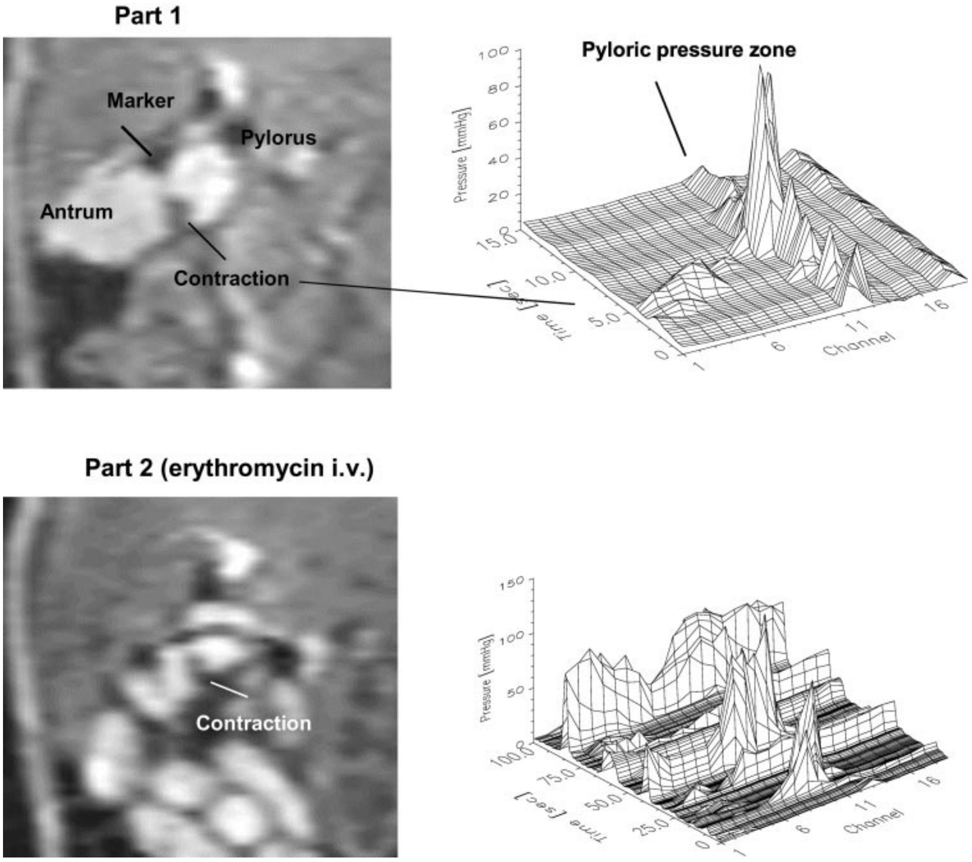

Fig. 2. MR images and pressure tracings of the antroduodenal area during intraduodenal nutrient infusion (*part 1*) and intravenous erythromycin infusion (*part 2*). The proximal marker and parts of the manometric assembly are visible and allow identification of the position of the sidehole chain of the assembly. In the pressure tracings, the horizontal axis depicts distance along the assembly, with 0 being the most proximal sidehole in the antrum. Intraduodenal lipid infusion led to a prominent pyloric band, whereas, after erythromycin, strong contractions occur in the antroduodenal area.

channel itself the mean pyloric pressure. In *part 2* of the study, a peak value of 60 mmHg was chosen as a threshold to characterize strong antral propagating pressure waves because pressure waves above this level were unique to the posterythromycin period.

*Contractile events and contraction waves (MRI).* For the analysis of antral contractions, MR motility scans at each time point were evaluated for speed of progression of the contraction, degree of lumen occlusion, and distance from the pylorus. The degree of occlusion of the gastric lumen by a contraction at any time point was measured and defined as the smallest distance between opposite sides of the gastric wall in the contracted state compared with the uncontracted state and expressed as a percentage. Contractions were characterized by their position relative to the assembly as well as by their speed, propagation, and degree of lumen occlusion. A contraction wave was defined as antegrade if its aborad propagation speed (determined by a linear fit of the displacement over time curve) exceeded 0.5 mm/s.

*Relating contractile events (imaging) to pressure events (manometry).* To relate geometric information to pressure changes, proximal and distal markers as well as the course of the assembly in the antropyloric region were identified in each image of a series of dynamic scans relative to the location of the pylorus. This was carried out without reference to the pressure data. The spatial location of pressure events and wall motion were defined as the points where the assembly and a virtual line connecting the opposing antral wall indentations intersected. During the motility scans, manometric data were subdivided in time into blocks of 1 s (8 digitized values) corresponding to the acquisition time of a single MR image. Because the resolution of the MRI (3 × 3 mm) was in the range of the manometric sidehole spacing (3.3 mm), the highest pressure of three adjacent manometry channels at the point of the wall indentation was defined as the pressure event produced by the wall indentation.

*Pyloric position in MR images and pressure tracings.* The position of the pylorus was tracked on the MR images by following the course of the catheter and measuring the distance along this curved line (over multiple adjacent images) to the proximal marker. This was compared with the manometrically identified pyloric channel, and deviations between these measures served as a measure of accuracy of the two methods.

### *Statistical Analysis*

Differences between pre (*part 1*)- and post (*part 2*)erythromycin data for AUC, GE, frequency of pressure waves, etc., were analyzed using Student's $t$-test (significance level $P < 0.05$) and are presented as means ± SD unless stated otherwise. Correlations (degree of lumen occlusion vs. strength of corresponding pressure event, speed of propagating waves measured by manometry vs. MRI, GE vs. antral motility) were tested using Pearson's correlation test and linear regression (significance level $P < 0.05$).

## RESULTS

### *Part 1: Gastric Motility During GE of Saline and Duodenal Infusion of Nutrients*

*Geometry assessment by MRI.* Six hundred one gastric wall indentations (contractile events) corresponding to sixty-two contraction waves were analyzed. All contraction waves were antegrade, and no lumen-occlusive contractions were observed in the antrum (degree of lumen occlusion: 47 ± 14%). In the MR images, the pylorus could be clearly identified in all scans as a 6- to 9-mm-thick structure separating antrum and duodenum (Fig. 2, *top*) and was observed to move forward and backward relative to the manometric assembly during antral contractions.

*Relationship between antral contractile and pressure events.* Two hundred fifty-four pressure events corresponding to fifty-one antegrade pressure waves were identified. The amplitude of pressure events was 12.5 ± 5.5 mmHg. Linear regression showed that the degree of lumen occlusion was only a minor causal factor contributing to the strength of a corresponding pressure event ($r^2 = 0.02$; $P = 0.026$; Fig. 3*A*).

*Relationship between propagating contraction and pressure waves.* Fifty-four percent (254/473) of antral contractile events were associated with a pressure event. The contractile events associated with detectable pressure changes had a lumen occlusion of 47 ± 15% compared with 43 ± 8% in those with no detectable pressure changes [$P$ = not significant (NS)]. However, 18% (11/62) of contraction waves observed by

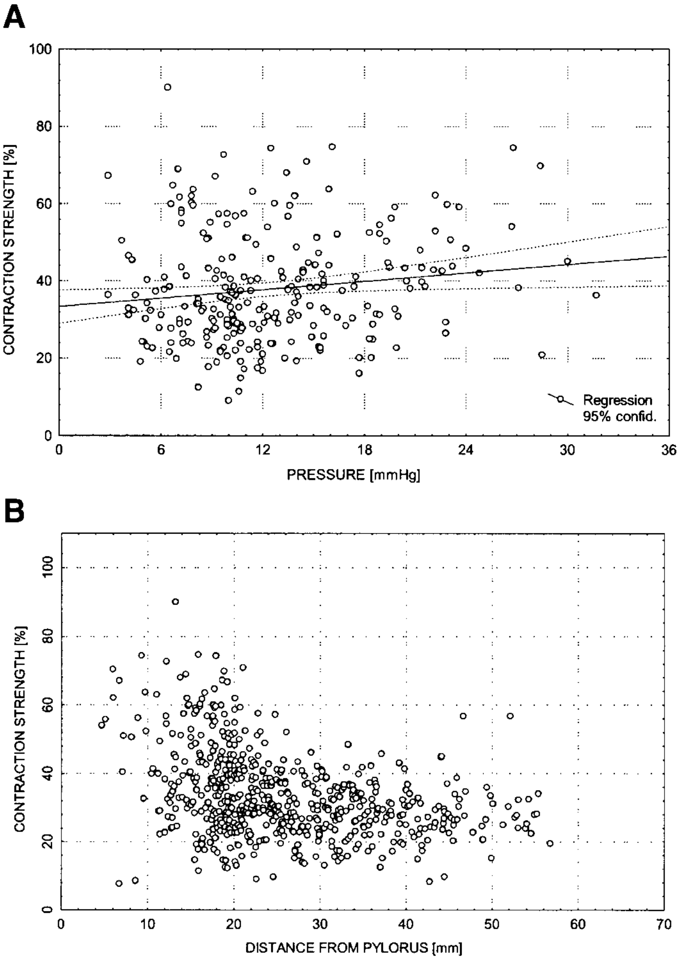

Fig. 3. *A*: relationship between the degree of lumen occlusion (i.e., contraction strength) as observed by MRI and manometric peak pressure. *B*: lumen occlusion of contractile events vs. distance from pylorus. Contractile events tended to be more lumen occlusive when approaching the pylorus.

MRI were not detected manometrically. The propagation speed was 2.7 ± 1.7 mm/s measured by MRI and 2.9 ± 1.4 mm/s by manometry ($r^2 = 0.23$, $P = 0.016$).

*Geometry of antral contractile events in relation to pyloric distance.* No significant correlation was found between the degree of lumen occlusion of a contractile event and its distance from the pylorus, even though stronger (i.e., more lumen occlusive) contractile events occurred when approaching the pyloric region (Fig. 3*B*).

*Pyloric pressure zone.* The position of the pylorus on the MR images coincided with a narrow (6–9 mm) zone of elevated pressure in the manometric recordings (pyloric pressure = 7.8 ± 2.9 mmHg; antral pressure = 3.7 ± 1.8 mmHg; duodenal pressure = 3.2 ± 1.5 mmHg). The deviation of the MRI-defined pylorus vs. the manometrically defined pylorus was 4.1 ± 0.6 mm, i.e., of the same magnitude as the MR image resolution ($3 \times 3$ mm$^2$, Fig. 4).

*Gastric emptying.* Median GE rate was 10.2 ml/min for the first 30 min (range: 4.4–14.2 ml/min). There was no correlation between the rate of GE and antral contractile activity analyzed by the AUC of antral pressure events ($r^2 = 0.03$, $P =$ NS; Fig. 5).

### *Part 2: Gastric Motility and GE During Intravenous Erythromycin*

*Geometry assessment (MRI).* In contrast to *part 1* of the study, strong antral contractions occurred in all subjects during erythromycin infusion (Fig. 2, *bottom*). The pylorus could no longer be clearly distinguished from the antrum by MRI, and tracking of the position of the manometric assembly could not be performed consistently.

*Antral pressure analysis.* Antral pressure activity was 17,562 (6,949–135,191; median, interquartile range) mmHg·s (expressed as AUC) compared with 5,939 (867–12,273) mmHg·s during the first 15 min of *part 1* without erythromycin ($P =$ NS). The frequency of antral pressure waves was 1.3 ± 1.2 vs. 1.9 ± 1.4 min$^{-1}$ (for $t = 0$–15 min of *part 1*; $P =$ NS); the speed of the pressure waves was 4.7 ± 2.2 vs. 4.0 ± 1.2 mm/s ($P =$ NS). In contrast to *part 1*, pressure waves with amplitudes >60 mmHg occurred (Fig. 5). There were large interindividual differences in the frequency of the waves exceeding 60 mmHg, which occurred at 0.7 min$^{-1}$ (median; range: 0.0–1.9 min$^{-1}$).

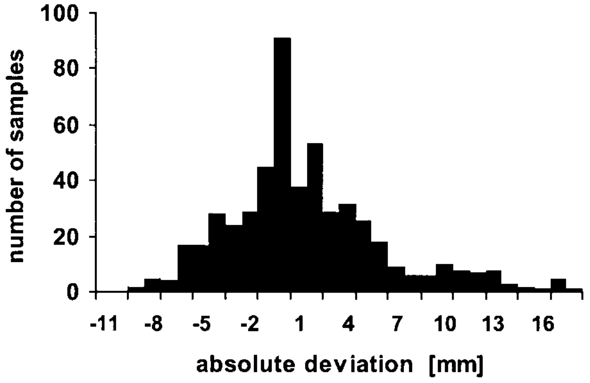

Fig. 4. The high-pressure band detected manometrically coincides well with the position of the pylorus as estimated from the dynamic MRI images.

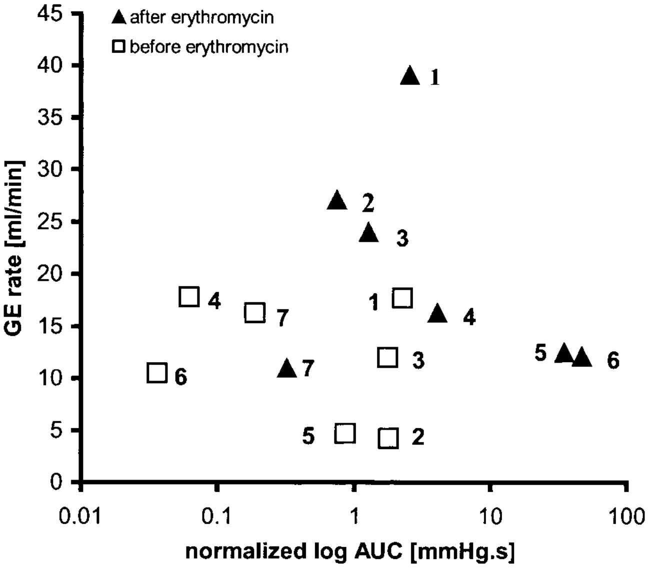

Fig. 5. Gastric emptying (GE) rate vs. antral motility [area under the curve (AUC) of pressure tracings] during *part 1* (during intraduodenal nutrient infusion) and *part 2* (after erythromycin infusion).

*Gastric emptying.* GE after erythromycin was 20.3 ml/min (range: 11.0–39.1 ml/min) compared with 11.9 ml/min (range: 4.2–17.8 ml/min for $t = 0$–15 min) during the first 15 min of *part 1* of the study ($P = 0.09$; NS). Relating GE to antral pressure activity (Fig. 4) showed a 22-fold increase in antral pressure activity in two subjects with slow GE (GE: 12.5, 12.1 ml/min; AUC: 32,529, 242,165 mmHg·s) compared with the other five subjects (GE: 24 ml/min, range: 11.2–39.1 ml/min; AUC: 8,762 mmHg·s, range: 2,222–28,217 mmHg·s). Although GE was low in these subjects, this difference in GE was not significant. Again, no correlation was found between GE and antral contractile activity ($r^2 = 0.26$, $P =$ NS; Fig. 5).

## DISCUSSION

This study used a combination of MRI and manometry to investigate antropyloroduodenal motor activity and its relation to GE during duodenal feedback inhibition of GE. The focus of this study was to determine the relationship between wall motion of the stomach and antral pressure recordings on a second-to-second basis. This question is important because most information on gastric motility is commonly obtained by manometry. First, we analyzed the sensitivity of manometry in detecting contractile events or contractile waves found on the MR images. Manometry missed <20% of the contraction waves detected by MRI. As the manometric system had a high sensitivity in detecting pressure changes (<0.5 mmHg), it is unlikely that we missed a high proportion of propagating pressure waves with significant impact on the pressure distribution in the intragastric lumen. Also, the degree of lumen occlusion of a contraction did not account for the events missed by manometry. In a closed fluid reservoir any uncompensated changes in (local) wall tension lead to pressure changes, but in the only partly filled stomach contractile events may not raise the overall pressure. Intraluminal pressure changes as a result of wall indentation did not depend on complete lumen occlusion, because most non-lumen-occlusive contractions also produced reliably detected pressure changes. In the case of lumen-occlusive contractions, the pressure tracing is a direct measure of the strength of the contraction. This was not true for the non-lumen-occlusive contractions in our study, for which we only found a weak correlation between the degree of lumen occlusion and pressure and no simple threshold for the ability of manometry to detect wall deformations. Rather, in the case of non-lumen-occlusive contractions, pressure is likely to be influenced by a combination of factors, such as the speed of the propagating wave, the depth of the contraction, the geometry of the antrum, and the contractile state of the pylorus.

The novel aspect of the present study is the direct correlation of local geometric information with the information from manometric tracings on a second-to-second basis while simultaneously assessing GE. Sidehole distances of 3.3 mm allowed detailed characterization of propagating antral pressure waves. To overcome the technical limitations of previous studies, we assessed a 3D portion of the antroduodenal region by multislice MRI (3-mm in-plane resolution), and the course of the catheter was tracked in the images to obtain the correct position of the manometric ports. Our study design and methodology did not, however, allow us to measure transpyloric flow directly, so we had to rely on the determination of the GE rate to evaluate the contribution of different motor mechanisms to emptying. Ultrasonography has been used to quantify transpyloric flow (6), showing that flow is mainly pulsatile and that forward and backward flow may occur during an antropyloric contractile sequence. The contractile state of the pylorus has been determined by videofluoroscopy (17). Simultaneous manometry showed that adequate assessment of the pyloric pressure band required a closely spaced sidehole array (~3 mm) of sufficient length to allow for movements of the pylorus. The use of videofluoroscopy, however, is limited by the ionizing radiation burden involved and does not allow assessment of GE. As yet, no methods have been established to measure GE, wall motion, and transpyloric flow simultaneously.

To examine the potential importance of non-lumen-occlusive contractions to GE, we used an intraduodenal nutrient infusion, which was previously shown to decrease antral propagating pressure waves and stimulate pyloric contractile activity (7). In this situation, we did not find a significant relationship between antral motility measured by manometry and GE. Furthermore, a separate analysis of the manometric data led to the conclusion that GE of nutrient liquids occurs primarily through a pressure pump mechanism controlled by pyloric opening during periods of relative quiescence in antral contractile activity (9). In agreement with other studies (2, 12, 13, 17), our results therefore indicate either that antral contractions are not primarily responsible for GE in this situation or that the commonly accepted parameters of antral motor activity (i.e., amplitude, frequency, propagation speed of pressure waves, antral motility indices) are not the most relevant.

There have been few studies examining the relationship between gastric intraluminal pressure and wall motion in humans, largely because of methodological limitations. An antral wall motion detector was combined with manometry to investigate how non-lumen-occlusive contractions were reflected in the manometric tracings (4). It was found that 89% of propagating antral pressure waves were associated with antral wall motion, which is comparable to the value found in our study (82%). The combination of manometry with imaging techniques provides an opportunity to examine the temporal and spatial organization of the individual motor mechanisms contributing to GE (8). In a previous study combining MRI and manometry, image information was used to count number and frequency of propagating contraction waves (18), finding a ratio of approximately three antroduodenal propagating contraction waves (MRI) for every two propagating pressure waves (manometry). However, no attempts were made to examine direct pressure-geometry relationships, and GE was not assessed. Limitations of this study included the manometric spatial resolution (10 mm). Furthermore, only a single slice was imaged by MRI, leading to problems in characterizing contractile events when the image plane was not located in the center of the antral lumen. Additional geometric information was extracted in a study comparing scintigraphic and manometric measurements of postprandial antral motility (11). Significant relationships were found between the amplitude of contractions assessed scintigraphically and the number of manometrically detected antral pressure waves in the distal antrum but not in the more proximal antral regions. Again, technical limitations (spatial resolution manometry: 15 mm; scintigraphy: 7 mm in a 2-dimensional projection) did not allow direct comparison between the amplitude of pressure and the corresponding contractile events.

Erythromycin altered the pattern of contractile events in the antrum. In agreement with previous studies (1, 5, 10), we observed episodes of strong antroduodenal activity after intravenous infusion of erythromycin. During high-antral-amplitude pressure waves, we found a completely contracted antropyloroduodenal region in the MR images. Strong contractions, i.e., a strong reaction to erythromycin, did not correlate with fast GE. This further supports the concept that GE is not simply proportional to the amplitude of pressure events or the occurrence of lumen-occlusive antral contractions (14). High-amplitude simultaneous contractions of the antroduodenal region after erythromycin could be responsible for abdominal cramps observed after intravenous erythromycin (3).

In summary, 3D dynamic information on wall motion obtained by MRI combined with pressure information from high-resolution manometry provides new information on the pressure-geometry relationship in the antropyloroduodenal region. We showed that although manometry detects ~80% of contraction waves, care must be taken when drawing conclusions from manometry recordings on actual contractile activity. The study further supports the notion that antral contractions alone do not reliably predict GE.

The study was supported by the Swiss National Science Foundation (SNF Grants 32-54056.98 and 31-55932.98) and the Kamillo-Eisner-Foundation, Hergiswil, Switzerland.

A separate analysis of the manometric data of *part 1* of this study was published previously (9).

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