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Interdigestive transpyloric fluid transport assessed by intraluminal impedance recording

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Savoye, G., C. Savoye-Collet, J. Oors, and A. J. P. M. Smout. Interdigestive transpyloric fluid transport assessed by intraluminal impedance recording. *Am J Physiol Gastrointest Liver Physiol* 284: G663–G669, 2003. First published December 18, 2002; 10.1152/ajpgi.00403.2002.—Our aim was to explore the use of intraluminal impedance recording for assessment of interdigestive transpyloric fluid movements. Twenty healthy volunteers were studied with a catheter allowing the recording of five antropyloroduodenal impedance signals simultaneously with six pressure signals. Patterns induced by air were verified by standard ultrasound. Transpyloric Doppler ultrasound was used to validate impedance patterns associated with transpyloric fluid transports. Impedance changes caused by air (short-lived increases) occupied 14 ± 12% of the time in the antrum and 0.8 ± 0.5% in the duodenum ($P < 0.005$). All fluid transport events lasting >4 s were recorded by both Doppler and impedance techniques. Transpyloric fluid transport was observed in all three phases of the antral migrating motor complex. The total number of transport events was significantly higher ($P < 0.05$) in *phase II* (18 ± 7) than in *phases I* (2.6 ± 2) and *III* (6.1 ± 3). Retrograde transport was observed mainly in antral *phase I* (54% of fluid movements, compared with 2.5% in *phase II* and 18.5% in *phase III*, $P < 0.05$). During *phase II*, 80 ± 13% of the impedance changes were associated with manometric events and 72 ± 9% of the antral contractions were associated with transpyloric fluid transport. Prolonged assessment of interdigestive transpyloric fluid transport events using intraluminal measurement of impedance is possible. Manometrically detectable contractions are the most frequent, but not the only, driving forces of these events.

multichannel impedance measurement; antroduodenal motility; Doppler ultrasound

NUMEROUS TECHNIQUES HAVE BEEN used to study transpyloric fluid movements including real-time ultrasound (17, 18, 28), Doppler ultrasound (8–10, 26), scintigraphy (15), fluoroscopy (4, 16, 27), and, more recently, magnetic resonance imaging (19, 22, 38). These tools have provided useful information, but all of these techniques require that the stomach be filled with either contrast agent or liquids, semiliquid, or solid meals. A full stomach excludes the study of normal interdigestive patterns (27). Moreover, use of these techniques is either limited by delivering irradiation, such as with scintigraphy and fluoroscopy, or by requiring a high level of expertise, i.e., the Doppler technique. Detailed and prolonged monitoring of the flow of fluid across the pylorus during the interdigestive state has long been impossible in humans.

The advent of intraluminal impedance measurement has made it possible to study interdigestive transpyloric fluid transport without the limitations imposed by stomach filling. Measurement of changes in impedance in the gastrointestinal tract involves application of a low-voltage potential difference to adjacent electrodes on a luminal catheter and measurement of the resulting current (32, 33). Passage of air or gas results in a temporary increase in intraluminal impedance, and passage of hyperconductive fluid results in a decrease in impedance (32, 33). Because an array of closely spaced electrodes is used, the direction in which boluses are transported (antegrade or retrograde) can be determined. Data obtained with impedance recording in the esophagus have already largely changed current opinions about gastroesophageal reflux (5, 6, 23, 29, 30, 31, 34–36). Although the feasibility of small intestinal impedance monitoring has been described (24, 25), studies using impedance measurement at the antroduodenal junction appear to have not been carried out yet.

The aim of the present study was to explore, in healthy volunteers, the use of intraluminal impedance monitoring for the assessment of interdigestive transpyloric fluid movements and to describe normal interdigestive patterns and their relationships with antroduodenal motility.

MATERIAL AND METHODS

Subjects

Twenty healthy volunteers (15 female, 5 male; mean age: 26 ± 7 yr; mean body mass index: 22.4 ± 3 kg/m^2) were studied after written informed consent was received from the volunteers. Subjects did not suffer from any gastrointestinal complaints, had not undergone major surgery in the past, did not suffer from any chronic disease, and did not use medication known to affect gastrointestinal motility. The study protocol was approved by the Human Research Committee of the Utrecht University Medical Center.

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Methods

Combined impedance and manometric recordings. Technology used in these studies involved combined monitoring of intraluminal impedance, intraluminal pressure, and transmucosal gastroduodenal potential difference. A perfused catheter was used that incorporates six side holes at 2-cm intervals (2 in the antrum, 1 in the pylorus, 3 in the duodenum) and six circular electrodes (2 in the antrum, 4 in the duodenum) positioned between side holes, yielding five impedance signals (Fig. 1). During the study, the catheter position was monitored continuously by measurement of the transmucosal potential difference (TMPD) between the distal antral side hole (A2) and the most proximal duodenal side hole (D1). Two TMPD channels were perfused with degassed saline from separate reservoirs at a rate of 0.2 ml/min. A disposable Ag-AgCl electrode attached to the forearm was used as the reference electrode. Pressures from the six perfused side holes and the five impedance signals were recorded using a dedicated stationary system (InSIGHT Stationary MII system; Sandhill Scientific, Denver, CO). For measurement of the impedance signals a 2-kHz current was used, which was passively limited to <8 μA. All signals were sampled at a rate of 10 Hz and stored on the hard disk of a computer for subsequent analysis.

Ultrasonography. Real-time ultrasound was used to assess the presence of air in the antroduodenal area. Real-time ultrasound images and transpyloric flow were assessed using a 2–4 MHz curved array probe (Esaote AUS; Pie Medical, Maastricht, The Netherlands) positioned at the level of the transpyloric plane with the antrum; the pylorus and the proximal duodenum were visualized simultaneously. Air was recognized as the presence of a hyperechoic mobile signal.

In seven volunteers, a pulse Doppler mode was used to measure flow velocity and timing. The sample volume of the pulsed Doppler was positioned across the pylorus, and the angle between the Doppler beam and the transpyloric direction of flow was always <60°. An episode of transpyloric fluid transport was defined as flow across the pylorus with a mean velocity of >10 cm/s lasting >1 s. Transpyloric fluid transport episodes were identified and the duration of each transpyloric fluid transport episode was measured during a 5-min period after the intake of 300 ml of water in seven volunteers.

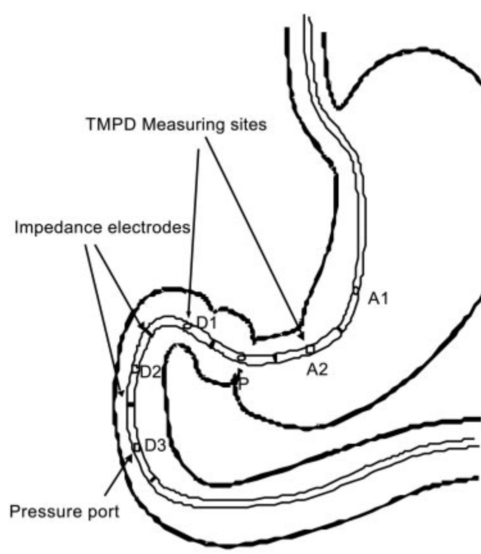

Fig. 1. Schematic representation of the catheter for combined pressure and impedance monitoring with 6 metallic rings at 2-cm intervals and 6 perfused side holes. TMPD, transmucosal potential difference. A1 and A2, antral side holes; D1–D3, duodenal side holes. P, pylorus.

Study protocol. After an overnight fast, the catheter was introduced transnasally and positioned across he pylorus. Subjects were studied in a supine position allowing 15° inclination. Catheter positioning by the use of TMPD measurement (and fluoroscopy if necessary) was followed by an accommodation period of 30 min. If during this period patterns suggestive of the presence of air in the antral area (high-impedance peaks) were observed, a check of the presence of air was done using standard ultrasound. Metal impedance ring electrodes were used as echoic marks to locate the probe. Thereafter, interdigestive recording took place until a complete cycle of the interdigestive migrating motor cycle (MMC) was observed. All 20 healthy volunteers were investigated to study normal impedance patterns and to assess the relationships between manometric and impedance patterns. In 7 of these 20 volunteers, transpyloric Doppler ultrasound was used to validate the impedance recordings of transpyloric liquid transport after they drank 300 ml of water at the end of the MMC recording. Impedance changes recorded during the first 5-min period after the water ingestion were compared with Doppler signals to assess concordance between both techniques. At the end of the experiment, 10 ml of air was injected into the duodenum through one of the duodenal channels, and the induced impedance patterns were recorded.

Data Evaluation

Analysis of the combined impedance and manometric recordings consisted of the following steps.

Visual analysis of the manometric recording. Visual analysis of the manometric recording was done only when antral TMPD was less than −20 mV, duodenal TMPD was greater than −15 mV, and the difference between the two was at least 15 mV, indicating correct positioning of the catheter (7). Visual analysis was used to identify the MMC phases. Antral *phase III* and duodenal *phase III* were detected in the antrum and duodenum. Antral *phase III* was defined as a burst of regular contractions lasting >1 min with a contraction frequency of 2.5–3.5 contractions/min, with a temporal overlap with duodenal *phase III*. Duodenal *phase III* activity was defined as regular contractions at a frequency of 10–12 contractions/min with at least 1 min occurring in all duodenal recording sites, antegradely propagated and followed by at least 5 min of relative quiescence (*phase I*). *Phase II* consisted of pressure waves >1.4 kPa occurring at a rate higher than 2 contractions/10 min and less than the maximum frequency of the antrum (3 contractions/min) or the duodenum (10–12 contractions/min). Propagation velocities of the antral pressure waves were calculated on the basis of the time of onset of the pressure rises. Contractions were considered to be related if the event in the more distal channel occurred between 5 s before and 10 s after the event in the more proximal channel.

Identification and characterization of bolus patterns: nature, presence time, and velocity. A drop in impedance was regarded as indicative of bolus transport across the pylorus when a drop in impedance to <40% of the baseline value was observed in at least three recording channels including one antral and one duodenal channel, implying presence in a 4-cm-long stretch. An arbitrary threshold of 40% was chosen, because use of the 50% threshold in the esophageal studies (32, 33, 35) appeared to lead to underdetection of fluid move-

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ments (see RESULTS), and respiratory variations in impedance baseline can reach 30% in the antroduodenal area. Impedance baseline was determined in the 5-s period immediately preceding the drop in impedance. Presence time of the bolus was measured as the time interval between the entry and exit point defined as when the point of the threshold of 40% of drop was reached (direction antegrade or retrograde). Velocity was measured from the entry points of the liquid bolus at the first and last level at which the drop was observed.

Analysis of the relationship between bolus and manometric events and MMC phase. During *phase II*, only antral pressure waves reaching the threshold of 2.8 kPa in at least one of the two antral channels were taken into account. Two impedance and manometric events were considered concomitant when they occurred within 10 s.

Statistical Analysis

When quantitative data were not normally distributed, comparisons of characteristics in impedance events between interdigestive phases were performed using the unpaired Mann Whitney *U*-test. The Wilcoxon signed-rank test was used for pairwise comparisons between concomitant impedance and manometric events recorded within the same 10-s period. For qualitative data, the χ-square test with Yates correction was used. Correlation between duration of liquid bolus assessed by both Doppler ultrasound and impedance and the correlation between impedance bolus front velocity and manometric pressure waves were tested by linear regression. A *P* value of <0.05 was considered statistically significant. Data from both manometry and impedance measurements were averaged and expressed as means ± SE.

RESULTS

Exploratory Observations

In the resting state, the antroduodenal impedance values were between 0.2 and 0.8 kΩ. Respiration-associated variations in impedance were seen in all subjects in *phase I*. These were characterized by simultaneous presence in all channels and lack of propagation (Fig. 2). During the 30-min accommodation period, high-amplitude rapid increases in impedance suggestive of the presence of air were seen in all subjects (Fig. 3). In all of the seven cases, where verified, concurrent

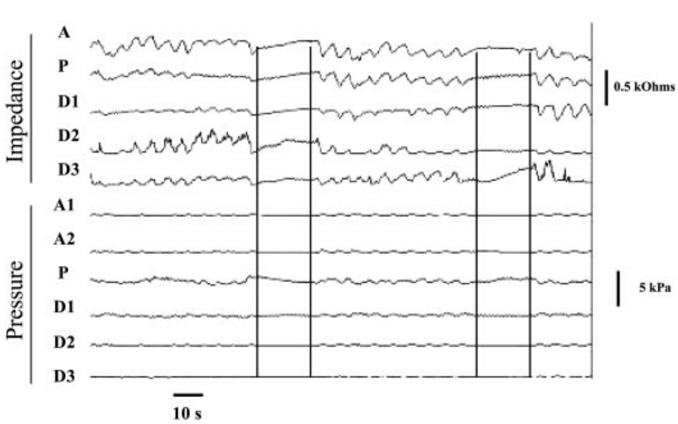

Fig. 2. Example of manometric and impedance signals showing the effect on two short apnea periods during *phase I* of the migrating motor complex on the impedance baseline signal.

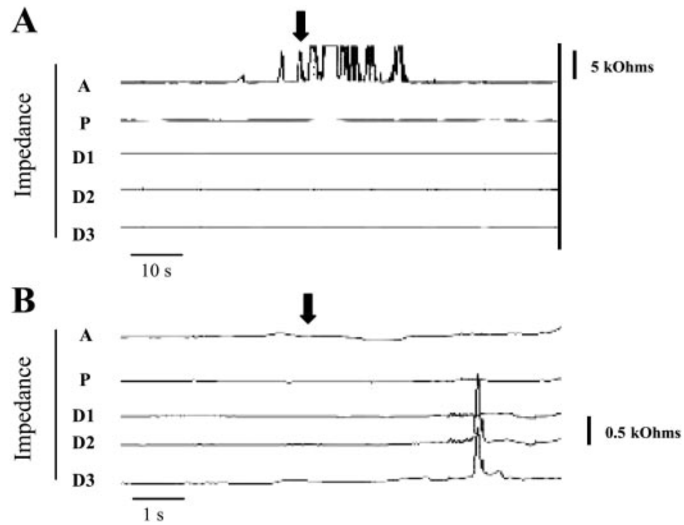

Fig. 3. *A*: example of impedance and pressure signals recorded from the antroduodenal area. A succession of high-amplitude impedance peaks (arrow) at the level of antrum was associated with the presence of an air bubble in the antrum at ultrasound examination. *B*: example of rapid and short-lived rises of impedance recorded at the duodenal level after the injection of 10 ml of air.

ultrasound evaluation showed that these impedance events were associated with the presence of air around the electrode rings. In all subjects, injection of air in the duodenum induced an immediate increase in impedance (between 0.5 and 3 kΩ), which was simultaneously recorded in two adjacent channels and was short-lived (always <3 s) as shown in Fig. 3. In seven individuals, concomitant Doppler ultrasound and impedance monitoring was carried out during 5-min recording episodes after the intake of 300 ml of water. In these tests, a total number of 15 propagated transpyloric drops in impedance to <40% of the baseline were seen, 14 of which were associated with a concomitant gastric emptying event recorded with the ultrasound Doppler probe (Fig. 4). During these tests, 24 Doppler events were recorded. All events that lasted longer than 4 s in Doppler (n = 11) were also recorded by the impedance probe. Only three of the five events with a duration between 2 and 4 s were associated with impedance changes, and none of the Doppler events lasting <2 s (n = 8) had an associated impedance change. When a threshold of 50% of the baseline was used, only 6 of the 14 concordant events were detected. Duration of the events recorded by Doppler ultrasound was 5.1 ± 2.3 s, and the duration of the impedance changes, defined as the interval between the entry and exit points, was 6 ± 2.9 s. It was not possible to associate a well-defined particular waveform in the impedance recordings with the retropropagated part of the Doppler signal recorded at the end of most of the gastric emptying events (Fig. 4).

Transpyloric Transport in the Interdigestive State

During 20 recording sessions, the catheter was in a correct transpyloric position during 75 ± 17% of the time. In total, 117 min of antral *phase III*, 258 min of

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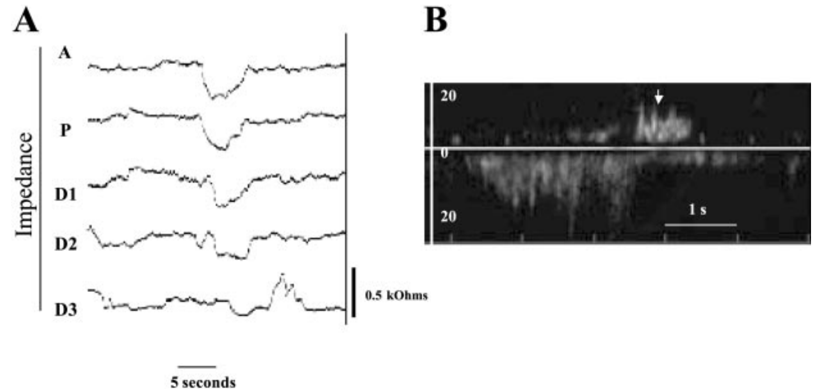

Fig. 4. Example of concomitant measurement of impedance signal (*A*) and Doppler signal (*B*) after drinking water. Scale on Doppler display is in centimeters per second. Arrow, retropropagated part of the Doppler signal recorded at the end of the gastric emptying event.

antral *phase I*, and 1,040 min of antral *phase II* were recorded. Mean phase durations were 16 ± 13 min for *phase I*, 63 ± 48 min for *phase II*, and 6.9 ± 3.2 min for *phase III*. Three MMC cycles lacked an antral *phase III* and only had *phase III* in the duodenum. Because none of these phases was associated with antegrade or retrograde transpyloric transport, these MMC cycles were discarded during further analysis. Patterns related to the presence of air were seen much more often in the antrum (14 ± 12% of the time) than in the duodenum (0.8 ± 0.5%) ($P < 0.005$).

Characteristics of bolus transport during each phase of the MMC are summarized in Table 1. Transpyloric fluid transports occurred in all of the three phases of the MMC. Presence of air in the bolus was unusual, especially during antral *phase III* in which it was observed in one individual only. The total number of transport events was higher in *phase II* (18 ± 7.2) than in *phase I* (2.6 ± 2.1) and *phase III* (6.1 ± 3.0) ($P < 0.05$). However, incidence of fluid transport events was higher ($P < 0.05$) in antral *phase III* (0.80 ± 0.5/min) than in *phase I* (0.13 ± 0.1/min) and *phase II* (0.36 ± 0.2/min). Retropropagated transport events were observed mainly during antral *phase I* (Fig. 5) in which they represented 54% of all transport events, compared with 2.5% in *phase II* and 18.5% in *phase III*. At least one retropropagated event was observed in each individual in *phase I*, whereas only 40% of the subjects exhibited a retropropagated event during *phase III*. All of the retropropagated events observed during *phase III* occurred at the end of the *phase III* when the antrum was already in *phase I*. In contrast, all of the antegradely propagated events in *phase III* were observed in the early *phase III* when both antrum and duodenum exhibited *phase III* manometric patterns. Mean durations of the fluid transport events were not different according to the phase of the MMC.

During *phase II*, 80 ± 13% of the changes in impedance observed were associated with manometric events, and 72 ± 9% of the antral contractions were associated with transpyloric fluid transports (Fig. 6). Only 60 ± 13% of the antral contractions in *phase III* were associated with transpyloric transports ($P < 0.05$ compared with *phase II*). In *phase II*, 282 impedance events were associated with an antral contraction (17 ± 12 associated events/subject), and 184 of these were suitable for the calculation of velocity of the associated antral pressure wave (pressure waves observed in 2 manometric channels). Mean velocity of the entry point of the impedance drop was 3.3 ± 2.3 cm/s, which was higher than the velocity of the associated antral pressure wave (1.1 ± 0.7 cm/s, $P < 0.05$). No correlation between both velocities was observed ($r = 0.12$, $P = 0.10$).

DISCUSSION

Our study has demonstrated that assessment of transpyloric fluid transport events using measurement of impedance is possible in healthy subjects and allows prolonged and well-tolerated recording without filling the stomach.

Table 1: *Characteristics of bolus transport during each phase of the migrating motor complex cycle in the gastric antrum*

Data	*Phase I*	*Phase II*	*Phase III*	Early *Phase III*	Late *Phase III*
Individual					
Number of events	2.6 ± 2.1*†	18 ± 7.2‡	6.1 ± 3.0		
Incidence per minute	0.13 ± 0.1*†	0.36 ± 0.2‡	0.80 ± 0.5		
Duration, s	6.5 ± 4.2	5.8 ± 5.1	5.9 ± 5.3		
Pooled					
Liquid, %	89	82	97.5	87.5	100
Air, %	11	18‡	2.5	12.5	0
Antegrade bolus, %	46*	97.5‡	81.5	100	0
Retrograde bolus, %	54*	2.5‡	18.5	0	100

Values are means ± SE. *$P < 0.005$ *Phase IA* versus *Phase IIA;* †$P < 0.005$ *Phase IA* versus *Phase III;* ‡$P < 0.005$ *Phase IIA* versus *Phase III.*

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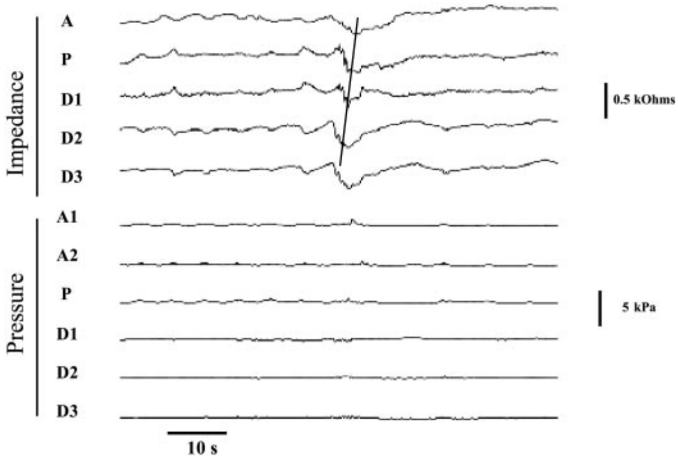

Fig. 5. Retrograde transpyloric liquid transport event recorded during *phase I* of the migrating motor complex.

To validate the changes in impedance observed in the interdigestive state, we used several techniques. For the air patterns, we recorded impedance after the intraluminal injection of 10 ml of air between two adjacent impedance electrodes. This induced a stereotyped increase in impedance, as in the esophagus (31, 33). Moreover, the hypothesis that spontaneously occurring short-lived increases in impedance are caused by air bubbles was proven to be correct by concomitant ultrasound, using the metallic rings located on the probe as echoic landmarks. For the validation of liquid patterns, we studied the passage of water across the pylorus that occurred after the ingestion of 300 ml of water. In all subjects, the impedance signals recorded showed well-defined propagated drops in impedance in the first 5 min after drinking water. When a concomitant Doppler examination was performed, it appeared that impedance patterns were always associated with Doppler signals lasting >4 s. For Doppler events of shorter duration, concordance between both techniques markedly fell, suggesting a higher Doppler sensitivity for detection of short-duration fluid transport events across the pylorus. However, both the design of the probe and the criteria used in the interpretation of impedance recordings could, in part, explain this discrepancy. In the present study, a drop in impedance was regarded as indicative of bolus transport when it was observed in at least three recording channels, including one antral and one duodenal channel, implying presence in a 4-cm long stretch, whereas Doppler assessed only the pylorus. In future studies, this specific issue should be addressed using a device with higher resolution, including a greater number of more closely spaced impedance rings.

The configuration of the impedance signals, recorded after drinking water, was used to analyze the recordings obtained without filling the stomach. Very similar impedance changes (amplitude, presence time, and velocity of the entry point) were observed during the interdigestive state. Intraluminal impedance monitoring is not a suitable technique for measurement of the volume of liquid transport; usually no relationship can be found between the volume of liquid transported and characteristics of the impedance changes (32). This point probably explains the absence of a difference in the present study between the impedance patterns associated with the gastric emptying of water and those related to the transpyloric passage of unknown volumes of interdigestive gastric secretion through the pylorus.

Previously published criteria (31, 33, 35, 36) for the analysis of esophageal impedance signals seem to be applicable to events observed across the pylorus, but in the latter area, a threshold of 40% seems to be better than 50%. Unfortunately, the characteristics of impedance changes at the gastroduodenal junction are not as well defined as those in the esophagus (31–33, 35). Various explanations could be proposed. First, the composition of the bolus at the level of the pylorus is variable. Second, the gas component described in the esophageal bolus seems to be very uncommon in the pyloric area in which air was present between 2.5 and 18% of the fluid movements. Third, lumen occlusion at the tail of the bolus by the oncoming peristaltic contraction as observed in the esophagus was very unusual in the present study. Furthermore, the shape of the last part of the impedance signal associated with an antral contraction may correspond to a temporal summation of a decrease induced by transpyloric liquid reflux as described by Doppler studies (10, 11) and an increase related to the propagated contraction at the tail of the bolus, leading to a wave configuration that is difficult to recognize. As a consequence of this, measured variables that are dependent on the exit point of the bolus, such as the presence time, must be considered with caution in the antropyloroduodenal area. For this reason, we decided to calculate the velocity of the head of the bolus instead of the tail. Lack of correlation between bolus and pressure wave velocity observed in this study might be related to this choice.

Our study also confirms previously reported observations on antroduodenal motor function. As expected, transpyloric fluid transport was observed during all three phases of the antral MMC. Antral contraction is

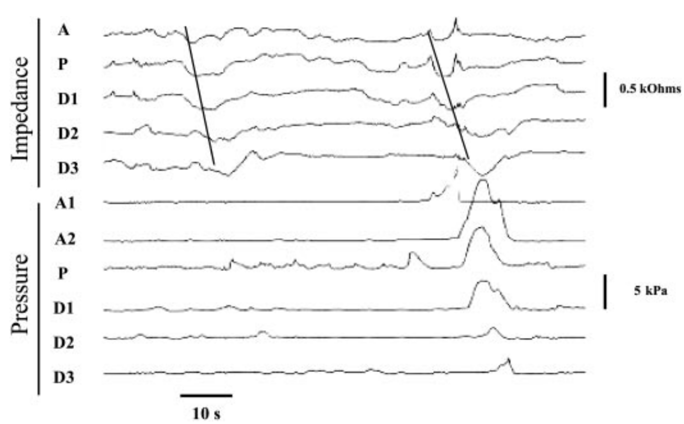

Fig. 6. Examples of transpyloric fluid transport events without manometrically detected-associated antral contraction (*left*) and with antral contraction (*right*).

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the most important, but not the only, motor of these events. Several studies on transpyloric transport carried out in the fed state tend to corroborate this finding. It is now clear that gastric emptying of a liquid meal is largely brought about during periods of relative motor quiescence of the antrum (14). Direct observation of transpyloric transport using Doppler ultrasound combined with antroduodenal pressure recordings has recently confirmed that emptying of a low-caloric meal is predominantly related to a low gradient in pressure between the antrum and the duodenum in the absence of antral peristalsis (11). By its opening, the pylorus acts as a gate, and the balance in pressure acts as a driving force, which allows both antegrade and retrograde transport by changing the direction of the gradient. In our study, the observation that in *phase I*, by definition a period without antral propagated pressure waves, transport events occurred in a comparable rate in both directions also suggests this pressure-related mechanism. Our observation that retrograde bolus transport is a frequent phenomenon in *phase I* is in accordance with the fact that in healthy subjects, *phase I* is associated with episodes of high pH in the antrum (37).

During *phase II* the majority of the fluid transport events across the pylorus are related to antral contractions. These transports are likely to be responsible for the duodenal acid exposition in *phase II* (37, 39). Arrival of acid from the stomach may stimulate duodenal chemical receptors and may trigger a duodenal clearance mechanism by stimulating duodenal motor activity. Nevertheless, a remaining 20% of liquid transport events occurred without detected manometric events. These transport events may be explained by a pressure-pump driving force like in *phase I*, but the low spatial resolution of the manometric device used in the present study, which allowed only two side holes in the antrum, could also explain this discrepancy. Moreover, as shown by Hveem et al, (13) only 86% of ultrasonically detected antral contractions are associated with a manometric event detectable somewhere in the antrum, even when a 10-lumen, perfused manometric assembly is used. The peristaltic driving force remains the most frequent mechanism responsible for interdigestive transpyloric fluid transports and seems also to be involved in fluid movements observed during *phase III* of the MMC. In our study, *phase III*, when originating in the antrum, was associated with early antegrade transport. This is the basis of the "housekeeping" function of *phase III*. Nevertheless, the majority of antegrade transport events occurred in *phase II*, which therefore could be seen as a second "housekeeper." However, because the frequency and number of events do not allow a reliable assessment of the volume transport, it could be argued that antral *phase III* remains the most efficient force to drive fluid across the pyloric gate, at least as far as the transported volume is concerned. Nevertheless, in our study, the percentage of antral contractions associated with bolus transport was higher during *phase II* than during *phase III*, suggesting that an integrated antropyloric motility pattern as in *phase II* is more efficient than *phase III* in allowing transpyloric fluid transport. During an antroduodenal *phase III*, the pylorus may act as a gate, which regulates the passage of fluids by allowing only a few gushes, when in temporal accordance with antral contractions (12, 20, 21), leading to a lower efficiency of antral contraction at that time than during *phase II*. Our finding that 72% of antral contractions is associated with transpyloric fluid transport confirms a major role for the antropyloroduodenal motor activity to induce transport. It is conceivable that contraction efficiency in terms of fluid transport could be affected in diseased conditions and that recognition of this disorder would offer a new pharmacological target in drug development.

Retrograde transport also occurred in *phase III* in 40% of individuals. These duodenogastric refluxes were observed during late *phase III* when the antrum was already in *phase I*. This observation confirms results of Bjornsson and colleagues who first described duodenal retroperistalsis in late *phase III* (1) and its association with noctural antral pH rises (2) and scintigraphically proved duodenogastric reflux (3).

In conclusion, application of impedance technology in the study of fluid transport across the pylorus is possible in humans and permits prolonged assessment of these fluid movements. When combined with manometry, it appears to be a promising new tool to increase pathophysiological knowledge in the complex antropyloroduodenal area.

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