Study of intestinal flow by combined videofluoroscopy, manometry, and multiple intraluminal impedance

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Imam, Hala, Claudia Sanmiguel, Brett Larive, Yasser Bhat, and Edy Soffer. Study of intestinal flow by combined videofluoroscopy, manometry, and multiple intraluminal impedance. Am J Physiol Gastrointest Liver Physiol 286: G263–G270, 2004.—Assessment of patterns of flow in the small bowel is difficult. Multiple intraluminal impedance has been recently used for study of flow dynamics in the esophagus. Our aims were 1) to validate multiple intraluminal impedance by correlating impedance events with intestinal flow as detected by fluoroscopy and 2) to determine intestinal flow patterns in the fasting and postprandial periods and their correspondence with manometry. First, six healthy subjects underwent simultaneous videofluoroscopic, manometric, and impedance recording from the duodenum. Videofluoroscopy was used to validate impedance patterns corresponding with barium flow in the fasting and postprandial periods. Next, 16 healthy subjects underwent prolonged simultaneous recording of impedance and manometry in both periods. Most flow events were short (10 cm or less), with antegrade flow being the most common. Correspondence between impedance and videofluoroscopy increased with increasing length of barium flow. Impedance corresponded better with flow, at any distance, than manometry. However, impedance and manometric events, when analyzed separately as index events, always corresponded with fluoroscopic flow. The fasting and postprandial periods showed comparable patterns of flow, with frequent, highly propulsive manometric and impedance sequences. Motility index was positively and significantly associated with length of impedance events. Phase 3 of the migrating motor complex could be easily recognized by impedance. Multiple intraluminal impedance can detect intestinal flow events and corresponds better with fluoroscopic flow than manometry.

METHODOLOGY

Validation study. SUBJECTS. Six healthy female volunteers (mean age 43 yr, range 24–51 yr) were studied. They had no gastrointestinal symptoms or abdominal surgery. Those of child-bearing potential used contraceptive methods. The protocol was approved by our institutional review board, and all subjects gave written informed consent.

EQUIPMENT. A custom-made catheter (Konigsberg Instruments, Pasadena, CA) was used for obtaining impedance and manometric data. The flexible, silicone-covered catheter had a diameter of 4.5 mm and a length of 200 cm. It contained five pairs of electrodes, with a distance of 2 cm between the two electrodes in each pair. A pressure sensor was positioned between two electrodes in each pair. The five electrodes and pressure sensor assemblies were spaced 5 cm apart, providing a total recording length of 20 cm. Another plastic tube, 1 mm in diameter, was attached to the catheter for infusion of barium (30 ml, concentration of 30%), with its tip just proximal to the first sensor assembly, in the second portion of the duodenum. This concentration of barium was shown to have no effect on intestinal motility (16). Videofluoroscopy was performed with an OEC C-arm with a rate of framing of 30/s (OEC General Electric Medical System, Salt Lake City, UT).

DATA ACQUISITION. The catheter was connected to a personal computer with specialized software (BioVIEW, Sandhill Scientific, Highlands Ranch, CO) for acquisition, analysis, and storage of impedance and manometric data and for graphic presentation. Synchronization of all signals during simultaneous videofluoroscopy, MII, and manometry was achieved by a custom-made device (Sandhill Scientific) placed within the fluoroscopy field. The device was connected both to the computer system that displayed the impedance and manometric

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tracings and to a control box placed on the patient’s chest. A signal delivered by the control box at the beginning of simultaneous recording could be traced to a single fluoroscopic frame and to a distinct mark on the tracing. Shielding the abdomen ensured that only a limited field of about 30 × 10 cm, which included the area involved by the catheter, was exposed to radiation.

Protocol. The catheter was introduced into the duodenum at the level of the junction between the duodenum and jejunum (Fig. 1G) after an overnight fast and under fluoroscopic control. It was then aligned along the lesser curvature, taped to the face to prevent migration, and connected to the computer for recording.

Forty minutes after the end of phase 3, barium was infused into the proximal duodenum and videofluoroscopic recording (15 ml) was obtained for 1 min. Dilute barium solution was infused over 30 s just before tapping, and the remaining half was infused during the first 30 s of recording. On completion of the recording, a liquid meal consisting of 500 ml of BOOST (720 kcal) was given. Another 1 min of recording was obtained, starting 45 min after ingestion of the meal.

Data Analysis

Videofluoroscopic, MII, and manometric data were initially analyzed separately and then synchronized for the correspondence between the three different types of events.

Videofluoroscopy. Records were analyzed visually. Patterns of flow were defined according to the movement of barium between sensor assemblies. We identified the following movements: 1) antegrade: forward transit of barium over various lengths; 2) retrograde: backward transit of barium over various lengths; and 3) back and forth: oscillating movement of barium between two assemblies without actual transit beyond the segment.

We analyzed each fluoroscopic event separately, including instances in which unrelated events occurred at the same time over the length of the catheter.

MII. A bolus of chyme, which normally has ionic elements, is expected to cause a drop in impedance baseline as it traverses the distance between each pair of ring electrodes. To determine the degree of drop that qualified as an event of flow, we analyzed all 12 MII events corresponding with fluoroscopic flow events that were observed to migrate aborally over five channel assemblies (Fig. 1F). We also analyzed all propagating sequences of MII and pressure events involving all five assemblies (96 during fasting and 183 in the PP period) encountered in part 2 of the study. This was done because analysis of data in part 1 showed that impedance events were always associated with flow over corresponding channels, as determined by fluoroscopy. This analysis showed that these MII events were characterized by a drop of 32 ± 10% below baseline; consequently, we determined that for an impedance event to be considered as associated with flow, it should have a drop of 12% or more below baseline (mean – 2SD). MII events were considered propagating if recorded in more than one channel and occurred within a time window that allowed a velocity of 0.2–3 cm/s between channels (25th to 75th percentile). This was based on analysis of all 21 propagating events found to correspond with fluoroscopic flow observed in the first study. Entry to entry values, defined as the 50% point between baseline impedance and its nadir, were determined for each pair of electrodes.

Manometry. Pressure waves (PWs) were considered to represent contractions if the rise in intraluminal pressure was ≥10 mmHg above the baseline (17). They were considered propagating if they were recorded in more than one channel and occurred within a time frame that allowed a minimal velocity of 0.7 cm/s and maximum velocity of 4 cm/s (30).

Correspondence of events. Correspondence was determined by the evaluation of simultaneous occurrence of all three types of events in corresponding channels and time frames. First, we used videofluoroscopy as the gold standard and determined the occurrence of pressure and impedance events at the time of fluoroscopic flow events. Then we used MII and manometry, in turn, as the index events and determined the occurrence of the other two events. This allowed us to determine the correspondence of MII and pressure events with flow as determined by fluoroscopy and then with each other.

Part 2

Prolonged recording of MII and manometry. METHODS. Sixteen healthy subjects (age range 20–51 yr, 9 females) were enrolled in this part, which consisted of simultaneously evaluating impedance and manometry. All subjects were studied after an overnight fast and intubated with the same probe used for part 1. The probe was advanced to the small bowel, and position was verified as described above.

Prolonged recording of MII and manometry. We measured phase 3 and analyzed a period of 30 min in phase 2, which followed the first observed phase 3, and thereafter a period of 30 min commencing 45 min after the same meal given in part 1. We chose this juncture because the fed pattern is well established at this time (27). Patterns of flow events by MII and pressure sequences by manometry were analyzed as described above.

Analysis. The total period of recording during fasting and after a meal was analyzed separately for the following: 1) comparison of patterns of flow, as determined by MII, between fasting and PP periods; and 2) correspondence between impedance and pressure events.

We arbitrarily elected to define the correspondence between pressure and impedance events as follows: 1) PWs and impedance changes that were seen in the same channels with equal numbers or 2) equal numbers of PWs and impedance changes but with PWs starting one channel above the impedance ones. Single PWs in channel 1 were excluded from analysis, because it is impossible to determine their proximal origination. Comparably, those in channel 5 were excluded because their distal extension could not be determined.

Statistics. The data were described using means ± SE for continuous variables that appeared to be normally distributed and using medians and interquartile ranges for those that did not. Categorical variables were described using counts and percentages.

The distributions of the lengths of the corresponding MII and pressure events were compared between the fasting and PP groups.
using a generalized estimating equations approach. The model accounted for correlation between the multiple measures per subject both over time within the two phase groups and between those two groups. Similarly, within-subject correlations were accounted for when testing for an association between motility index and length of MII propagation. This was done after stratifying for the length of propagating pressure events, thus performing five subanalyses, one each for pressure sequence length, from one to five channels. This analysis was performed using a mixed model analysis of variance. Both analyses used an autoregressive one-covariance matrix to model the within-subject correlations. Motility index formula = In(amplitude × number of contractions + 1) (3).

*P* values ≤0.05 were considered statistically significant. All reported *P* values were two-sided without adjustment for multiple comparisons. All analyses were performed using SAS software (Unix version 8.0; Cary, NC).

**RESULTS**

**Study 1**

Impedance baseline (based on all impedance events analyzed) was 396.2 ± 95.5 Ω. The drop of the impedance baseline to the nadir matched the arrival of the barium bolus to the corresponding channel. The rise of impedance from the baseline to the nadir back to the baseline coincided with bolus clearance on the corresponding channel. The rise of impedance from the baseline to the nadir matched the arrival of the barium bolus to the proximal jejunum. Phase 2 and PP periods showed comparable patterns of PWs. Impedance baseline (based on all impedance events analyzed) was 396.2 ± 95.5 Ω. The drop of the impedance baseline to the nadir matched the arrival of the barium bolus to the corresponding channel. The rise of impedance from the baseline to the nadir back to the baseline coincided with bolus clearance on the corresponding channel. The rise of impedance from the baseline to the nadir matched the arrival of the barium bolus to the proximal jejunum. Phase 2 and PP periods showed comparable patterns of PWs.

**Videofluoroscopy.** The types of flow, observed by videofluoroscopy, are presented in Fig. 2. Antegrade flow events predominated overall. Most flow events were short, extending over a distance of <10 cm. Whereas antegrade flow extended over various lengths, retrograde flow did not exceed 10 cm (Table 1). Of interest were the long antegrade flow events, involving all five channels. All such events extended well beyond the most distal channel, showing a PW that propelled the barium into the proximal jejunum. Phase 2 and the PP period showed comparable patterns of PWs. Impedance changes were also comparable, suggesting common patterns of flow. The videofluoroscopic flow was taken as the gold standard, and its correspondence with impedance and manometric events is presented in Table 1. Longer flow sequences showed greater correspondence with impedance and manometric events. Antegrade flow events showed a stronger correspondence with MII and manometric events than retrograde ones. Also, the videofluoroscopic correspondence with impedance was higher than that with manometry at any given length of flow.

**MII as index event.** When impedance events were analyzed first and considered the gold standard, we found that every impedance event corresponded with a videofluoroscopic flow. However, only 62% of impedance events corresponded with manometric events.

**Manometry as index event.** When manometric events were analyzed first and considered the gold standard, we found that every manometric event, whether stationary or propagating, corresponded with a videofluoroscopic flow. However, only 72% of manometric events corresponded with impedance events.

**Study 2**

**Phase 2 and PP periods.** The distribution of all MII and manometric events, per subject and according to length, is presented in Table 2. The distribution of all MII and manometric events and their correspondence with one another is presented in Tables 3 and 4. Short events predominated in both periods, and all events were more frequent in the PP period. However, the distribution of events according to length was comparable between fasting and PP periods in both MII and manometry. The correspondence between the two types of events increased as their length increased. We observed a total of 279 MII sequences involving all five channels. Correspond-

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**Table 1. Types and lengths of fluoroscopic flow events and percentages of correspondence with MII and manometric events**

<table>
<thead>
<tr>
<th>Type and Lengths of Movements, cm</th>
<th>Total Number of Events Per Subject</th>
<th>MII, %</th>
<th>Manometry, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antegrade &lt;5</td>
<td>83</td>
<td>12.5</td>
<td>51.8</td>
</tr>
<tr>
<td>Retrograde &lt;5</td>
<td>75</td>
<td>12.5</td>
<td>37.3</td>
</tr>
<tr>
<td>Antegrade 5–9</td>
<td>39</td>
<td>6</td>
<td>69</td>
</tr>
<tr>
<td>Retrograde 5–9</td>
<td>4</td>
<td>0.5</td>
<td>25</td>
</tr>
<tr>
<td>Antegrade 10–14</td>
<td>9</td>
<td>1.5</td>
<td>100</td>
</tr>
<tr>
<td>Antegrade ≥15</td>
<td>12</td>
<td>2</td>
<td>83</td>
</tr>
<tr>
<td>Back and forth</td>
<td>38</td>
<td>6</td>
<td>23.6</td>
</tr>
</tbody>
</table>

Data for no. of events presented as median and interquartile range (in parentheses). MII, multiple intraluminal impedance.

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**Table 2. The distribution of MII and manometric events (pressure waves) per subject, according to length, in the fasting and postprandial periods**

<table>
<thead>
<tr>
<th>Length, cm</th>
<th>MII</th>
<th>Pressure Waves</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>21</td>
<td>49.5</td>
</tr>
<tr>
<td>5–9</td>
<td>9.5</td>
<td>23</td>
</tr>
<tr>
<td>10–14</td>
<td>8</td>
<td>16.5</td>
</tr>
<tr>
<td>15–19</td>
<td>8</td>
<td>11.5</td>
</tr>
<tr>
<td>≥20</td>
<td>5.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Data presented as median and interquartile range.
The distribution of total manometric events (PWs) according to length in the fasting and PP periods and their correspondence with the manometric events (PWs)

<table>
<thead>
<tr>
<th>Length, cm</th>
<th>MII events, % of total</th>
<th>Correspondence with PWs, %</th>
<th>MII Events with no PWs in any channel, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>277 (43.8)</td>
<td>27.8</td>
<td>59.7</td>
</tr>
<tr>
<td>5–9</td>
<td>143 (19.3)</td>
<td>47.6</td>
<td>20.7</td>
</tr>
<tr>
<td>10–14</td>
<td>129 (16.0)</td>
<td>33.3</td>
<td>8.9</td>
</tr>
<tr>
<td>15–19</td>
<td>118 (12.5)</td>
<td>47.5</td>
<td>5.7</td>
</tr>
<tr>
<td>≥20</td>
<td>96 (8.4)</td>
<td>77.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Total</td>
<td>763 (100)</td>
<td></td>
<td>1,689 (100)</td>
</tr>
</tbody>
</table>

PP, postprandial; PW, pressure wave.

The primary function of the small bowel is proper mixing and propulsion of chyme and absorption of nutrients. Fasting and PP patterns of small bowel motility (6, 9, 10, 26–28, 30) promote this function by ensuring timely and appropriate flow of contents, thus avoiding the consequences of stasis or rapid transit. These patterns are determined largely by manometry, making use of intraluminal measurement of pressure events. Manometry, however, has limitations. Most importantly, whereas the different periods described above are easily recognizable, they provide only limited and indirect information regarding the pattern of individual flow events that ultimately determine the movement of chyme along the intestine. Consequently, these flow patterns remain poorly understood. As a clinical tool, manometry is helpful in the diagnosis of intestinal dysmotility. However, it distinguishes poorly between various types of dysmotility syndromes because they share common manometric features (3, 9). There is also poor correspondence between manometric patterns and symptoms (31). MII may overcome some of these limitations. Although MII has been tested in the small bowel, it was not validated, and comparison with manometry was not attempted (13, 14).

The first part of our study was primarily designed to validate the changes in impedance by performing a simultaneous recording of MII and fluoroscopy, considered the gold standard for assessment of flow in the bowel. This part, with the addition of manometry, also allowed the assessment of temporal and spatial relationship between events recorded by the different techniques during fasting and following a meal. Fluoroscopy showed that most flow events, whether antegrade or retrograde, extend over a short distance of 10 cm or less, with antegrade...
events being more predominant. These findings are supported by Andrews et al. (1), who, by using manometry, observed that antegrade sequences were more common than retrograde ones and that most sequences were over distances of 3–5 cm. Fluoroscopy showed that whereas antegrade events extended over various distances, retrograde flow occurred over distances that did not exceed 10 cm (Fig. 2). This finding is supported by previous studies (4, 8) using manometry and duplex sonography techniques. When examining correspondence of manometric events with fluoroscopy, we observed that most short retrograde flow occurred as a result of a single PW that either split the flow in antegrade and retrograde direction or generated just retrograde flow. In accordance with the findings reported by Rao et al. (16), back and forth movements on fluoroscopy corresponded very poorly with the other two events and the least so with manometry.

The most important findings of the first study were validation of impedance events by MII and the correspondence between the three types of events. This was done by considering each of the techniques, in turn, as the index one and then determining its correspondence with events detected by the other two techniques. Importantly, impedance events were more likely than manometric ones to be associated with fluoroscopic flow, regardless of the type of flow or its distance (Table 1). The correspondence of both events with antegrade fluoroscopic flow was stronger the longer the distance of fluoroscopic flow event. The correspondence between MII and fluoroscopy for antegrade fluoroscopic flow ranged between 51.8 and 100%, likely reflecting the fact that the intestinal lumen did not completely clear the barium; thus the remaining conductive contents may minimize changes in impedance baseline, a limitation of this technique. However, longer MII sequences associated with higher motility index (Fig. 3, A–E), suggesting better lumen clearance and hence better detection by MII. When MII and manometric events were analyzed as the index event, they always corresponded with fluoroscopic flow but only corresponded with one another in two-thirds of the cases. The reason for this observation is not clear. However, one may speculate that changes in bowel tone, not detected by intraluminal sensors, may generate flow without PWs. Conversely, PWs may occur in the absence of changes in MII, perhaps because of incomplete emptying of luminal contents. This is

Fig. 3. Correlation between length of MII event sequence (in cm) and the motility index of PWs in the corresponding channels (presented as the average motility index per channel). A–E: length of pressure sequences analyzed, from a single PW (A) to a sequence of 5 propagating PWs (E). The means ± SE value in each figure indicate the rise in motility index required for an increase of MII propagation by 5 cm.
supported by the observation that PWs commonly do not clear the lumen completely, as discussed above. These two observations indicate that MII is more sensitive than manometry in detecting flow events. Whereas flow may be undetected by MII when using the study criteria, every MII event seen corresponded with fluoroscopic flow. This is important in the analysis of routine tests, done without the simultaneous use of fluoroscopy, as done in the second part of the study.

Whereas impedance events and bolus transport points (entry, transit, and exit) in the small bowel, as indicated by fluoroscopy, resembled those in the esophagus (24, 25), a number of differences was noted. Impedance baseline in the small bowel is far lower than that in the esophagus, perhaps explained by the presence of intestinal secretions and gastric contents, which are conductive in nature. This is supported by the finding that pressure sequences, even those conducted over long distances, rarely cleared the intestine completely of barium. Also, unlike the esophagus, the exit of bolus, as determined by the increase in impedance from the nadir to baseline, did not always coincide with the upstroke of the PW, which was observed to happen along the nadir (Fig. 1, A–E). This finding was also reported in MII studies of the antrum (19).

The second part of our study served to obtain extended recording of simultaneous MII and manometry during the fasting and PP periods. As expected, both manometric and impedance events were more numerous in the PP period compared with the fasting one. Comparable with the first study, short events predominated in both periods. Comparable with the first study, the correspondence between MII and manometric events was stronger the longer the distance of the event (Table 3 and 4).

Of particular interest were the long sequences of MII involving all five channels. In all of them, barium was seen to flow well beyond the end of the catheter, suggesting that these sequences are highly propulsive. In the second study, we observed comparable proportion of such long sequences in the fasting and PP periods, although the absolute number was much higher postprandially. Approximately half of such MII sequences were associated with migrating sequences of intraluminal PWs. Similar long PW sequences were described by Sarna et al. (17). The highly propulsive nature of these sequences may explain why conditions with reduced phase 2 activity, such as postoperative states (2), somatostatin (29), or opiates (15), are associated with delayed small bowel transit, despite the normal presence of phase 3. Thus these sequences may be as important to the normal gut homeostasis as phase 3. It also explains the finding of comparable rate of transit of liquid in the jejunum in phase 2 and the PP period (18). This was also supported by studies in dogs (7, 20), using videofluoroscopy and manometry, showing that these propagating PWs were responsible for most of the aboral propulsion of intestinal chyme. These long MII sequences were observed with PW sequences of variable length, suggesting that recording of pressure events can underestimate even flow events of substantial length.

Phase 3 sequences were easily recognized by MII (Fig. 4). This is important because the presence of phase 3 and its propagating pattern are among the most common criteria used in the evaluation of small bowel manometry (9). Interestingly, long MII events were commonly observed just before phase 3, and impedance changes during phase 3 showed regular fluctuation correlated with PWs. Perhaps the long duration of the normal phase 3 sequence is required to ensure the clearance of poorly digestible material, which may not be easily cleared by a single sequence of propagated PWs.

In conclusion, measurement of impedance can be applied to the small bowel and can be incorporated in existing manometric probes used for pressure measurements. This technique provides useful information on the pattern of flow in the small bowel not obtained by manometry. MII promises to expand our knowledge of small bowel motor function in health and disease.
REFERENCES


