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CLINICAL RESEARCH

Postprandial transduodenal bolus transport is regulated by complex peristaltic sequence

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Abstract

AIM: To study the relationship between the patterns of postprandial peristalsis and transduodenal bolus transport in healthy subjects.

METHODS: Synchronous recording of chyme transport and peristaltic activity was performed during the fasting state and after administration of a test meal using a special catheter device with cascade configuration of impedance electrodes and solid-state pressure transducers. The catheter was placed into the duodenum, where the first channel was located in the first part of the duodenum and the last channel at the duodenojejunal junction. After identification of previously defined chyme transport patterns the associated peristaltic patterns were analyzed.

RESULTS: The interdigestive phase 3 complex was reliably recorded with both techniques. Of 497 analyzed impedance bolus transport events, 110 (22%) were short-spanned propulsive, 307 (62%) long-spanned propulsive, 70 (14%) complex propulsive, and 10 (2%) retrograde transport. Short-spanned chyme transports were predominantly associated with stationary or propagated contractions propagated over short distance. Long-spanned and complex chyme transports were predominantly associated with propulsive peristaltic patterns, which were frequently complex and comprised multiple contractions. Propagated double wave contraction, propagated contraction with a clustered contraction, and propagated cluster of contractions have been identified to be an integralted part of a peristaltic sequence in human duodenum.

CONCLUSION: Combined impedancometry and manometry improves the analysis of the peristaltic patterns that are associated with postprandial transduodenal chyme transport. Postprandial transduodenal bolus transport is regulated by propulsive peristaltic patterns, which are frequently complex but well organized. This finding should be taken into consideration in the analysis of intestinal motility studies.

Key words: Transduodenal bolus transport; Organization of duodenal peristalsis; Combined impedance manometry

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INTRODUCTION

The spatial and temporal organization of gastrointestinal contraction waves seems to be a more important determinant of the flow of luminal contents than their number and amplitude[1,2]. Therefore, significant advances in understanding intestinal motility disorders could be made by analysis of bolus movement together with peristaltic activity within the gastrointestinal lumen. With manometry alone small intestinal motility patterns can be obtained[3]. However, up to date there are limited observations on the relationship between intestinal chyme transport and peristaltic activity in humans because fluoroscopic studies are limited due to radiation exposure.

Multichannel impedancometry is a newly developed technique to study chyme transport[4]. We performed human studies and demonstrated that multichannel impedancometry is a reliable technique to obtain detailed information about spatial and temporal chyme movements, both in the human esophagus and duodenum[5-9]. Simultaneous impedancometry and pH-monitoring have also been used for characterisation of patterns of gastroesophageal reflux[10,11].

In previous studies we have characterized postprandial duodenal chyme transport patterns[5,6]. Recently, we developed the technique of combined impedancometry and manometry (CIM)[12] and applied it for motility testing in healthy subjects and reflux patients[13-15]. In the present study we used this approach in order to systematically study the relationship between intestinal chyme transport patterns and peristaltic patterns and to obtain detailed information about peristaltic mechanisms regulating postprandial transduodenal bolus transport.

MATERIALS AND METHODS

Subjects

Ten subjects (7 males and 3 females, mean age 34 years, range 26-36 years) were studied after written informed consent. All healthy volunteers were recruited from the medical staff. They took no medication and had no history of gastrointestinal disease. The study protocol was approved by the local ethical committee of Aachen University.

Methods

Combined impedance and pressure recording: A custom-made combined catheter consisting of 11 impedance segments (each 2 cm long) and 4 semiconductor pressure transducers was used (prototype developed by Dr. Nguyen RWTH-Aachen, Ref. 13). The pressure transducers were located between the impedance channels 1-2, 4-5, 7-8 and 10-11 (intertransducer distance 6 cm) (Figure 1). The cascade configuration of the impedance electrodes allows continuous monitoring of chyme movement and is particularly suitable for analysis of chyme transport patterns[5,6].

Study protocol: After an overnight fast from 10 pm, the catheter was placed transnasaly into the duodenum under fluoroscopic control. All channels were placed in the duodenum. The proximal end of the catheter was located in the first part of the duodenum and the last channel at the duodenojejunal junction (Figure 1). This catheter position yielded information about bolus transport along the whole duodenum. The final position was confirmed by fluoroscopy at the beginning of the studies.

Synchronous recording of chyme transport and peristaltic activity was started after a resting period of at least 20 min following catheter placement. After identification of a phase 3 migrating motor complex, a standard test meal consisting of 500 g of commercially available yogurt with small pieces of fruit (450 kcal, 400 mL, 5.5 g fat, 12.5 g protein, 75 g carbohydrate) was administered, and data were collected for a further 2 h.

Statistical analysis

Impedance and manometry tracings were reconstructed on screen and the patterns were consecutively analyzed. Since we studied transduodenal bolus transport, only impedance signals related to a complete chyme transport over at least 6 cm beginning at the first impedance channel were included and analyzed as previously described as a bolus transport event (BTE)[5,6]. This definition was used to exclude transpyloric movement of gastric contents into the duodenum bulb without initiation of duodenal peristaltsis. BTE were classified according to (a) site of onset (proximal *vs* distal), (b) propulsion direction (propulsive *vs* retropulsive), (c) propagation distance (short-spanned ≤ 8 channels or ≤ 16 cm *vs* long-spanned > 8 channels or > 16 cm), (d) number of components (simple = one component *vs* complex = multiple components). Thus the transport patterns were: (a) short-spanned propulsive, (b) retrograde, (c) long-spanned propulsive, and (d) complex propulsive[5,6,8]. Of note, our previous validation study[6] demonstrated that long-spanned BTE are associated with a significant drop of intraluminal pH and change of electrical conductivity, thus indicating real chyme movement originating from the stomach.

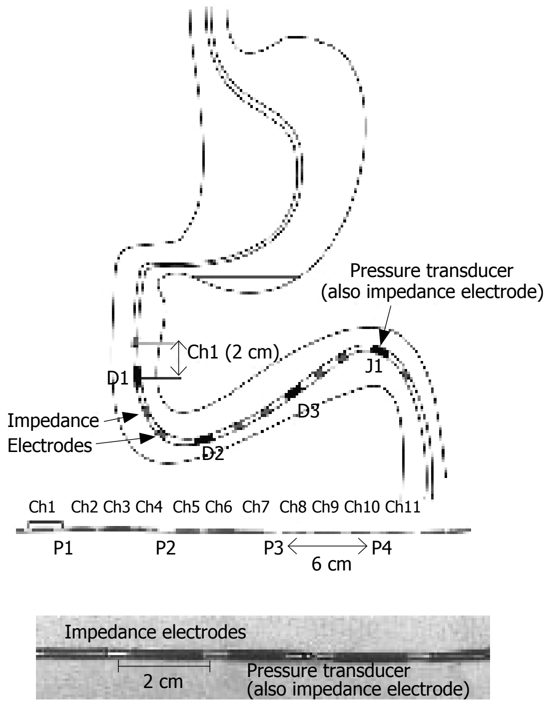

Figure 1 Modified manometry catheter for concurrent impedance-manometry procedure. The 4 semiconductor solid-state pressure transducers (P1-P4) serve also as impedance electrodes and are placed at 6 cm distance each. The 8 impedance electrodes (4 mm length) are arranged between the pressure transducers at a distance of 16 mm. Together with the pressure transducers, they form 11 impedance segments, each 2 cm long (Ch1-Ch11). The solid-state pressure transducers are located exactly between the impedance channels 1-2, 4-5, 7-8, and 10-11, respectively. The first channels were located at the first part of the duodenum.

After identification and classification of the chyme transport patterns the corresponding peristaltic sequences were analyzed. Firstly, the peristaltic nature of the associated contractions was characterized as (a) stationary (isolated contraction observed in only one channel) or (b) propagated (contraction detected over 2, 3 or 4 pressure channels = 6, 12 and 18 cm). Secondly, propagated contractions were classified according to Summers *et al*[16] to be: (a) propagated contraction with single wave contraction (1 contraction), (b) propagated contraction with a double wave contraction (2 contractions) or propagated contraction with a clustered contraction (> 2 contractions occurring at a rate of 5 s) (c) propagated cluster of contractions (clustered contractions occurring at more than one pressure channel) as shown in Figure 2. A double spike wave was considered to be single wave. Contractions that were observed between the BTEs were not included for analysis. Data are expressed as total number of events counted.

RESULTS

Combined impedance-manometry during the interdigestive state

During the interdigestive phase 2 there were irregular motility activities as recorded by manometry and irregular chyme transport events as recorded by impedance-manometry (Figure 3, upper panel). Both impedance and manometry recorded the same features of the phase 3 complex (Figure 3, lower panel).

Combined impedance-manometry during the postprandial state

The postprandial manometry tracings showed irregular peristaltic activity, which is difficult to analyse (Figure 4, upper panel). However, with combined impedance and manometry the relationship between transduodenal bolus transport event and associated peristaltic activity could be investigated in more detail (Figure 4, middle panel). Plotting the tracings at high resolution, the patterns of chyme transport as recorded by impedance and of peristalsis as recorded by manometry were analysed systematically (Figure 4, lower panel).

Impedance bolus transport patterns

A total number of 564 BTEs were counted. Sixty seven BTEs (12%) were excluded, because they could not be clearly classified according to the impedance criteria. Of the remaining 497 BTEs the distribution of the impedance patterns was: (a) short-spanned propulsive transport, 110 events (22%), long-spanned propulsive transport, 307 events (62%), and (d) complex transport, 70 events (14%) and retrograde transport events, 10 (2%).

Relationships between impedance transport patterns and manometry peristaltic patterns

The relationship between impedance transport patterns and manometry peristaltic patterns could be classified as followed (Figure 5): (a) of the short-spanned propulsive chyme transports (110 events) the majority of them was associated either with a stationary contraction (43 events or 39%) or a single contraction propagated over only 2 pressure channels (64 events or 58%); (b) all long-spanned propulsive chyme transports (307 events) were associated with a propagated contractions; (c) all complex chyme transport patterns (70 events) were associated with propagated contractions, particularly over 4 pressure channels; (d) retrograde chyme transport was rare (10 events) and are associated either with a stationary contraction (7 events) or retrograde propagated single wave contraction (3 events).

Of the long-spanned bolus transport events (307 events), 92 BTEs (30% of them) were associated with a propagated contraction over 2 or 3 pressure channels (6 -12 cm), and 215 BTEs (70% of them) were associated with a propagated contraction over 4 pressure channels (18 cm).

Of the long-spanned propulsive chyme transports over 4 channels (215 events), 61 events (28% of them) were associated with a propagated single wave contraction, and 154 events (72% of them) were associated with a propagated double wave contraction or a propagated contraction with a clustered contraction. None of these bolus transport was associated with a propagated cluster of contractions.

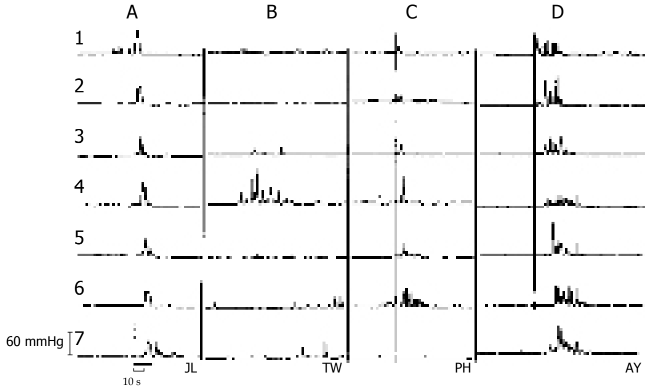

Figure 2 Classification of the peristaltic patterns according to Summers *et al*[16]. The peristaltic pattern can be classified to be (A) propagated single (double spike) wave contraction, (B) isolated (stationary) cluster of contractions, (C) propagated contraction with a clustered contraction, and (D) propagated cluster of contractions.

All complex propulsive chyme transports (70 events) were associated with propagated contractions over 4 channels (18 cm): 48 events (68% of them) were associated with a propagated double wave contraction or a propagated contraction with a clustered contraction, and 22 events (32% of them) were associated with a propagated cluster of contractions. None of these bolus transport was associated with a propagated single wave contraction.

Examples of the bolus transport events and their associated peristaltic patterns are shown in Figures 6-8.

DISCUSSION

Only few studies in man have directly analysed the spatial and temporal relationship between the patterns of chyme flow and patterns of peristaltic contraction waves in the duodenum, particularly during the postprandial state and in details. This study was performed to directly address this issue using the newly developed and validated technology of combined impedance and manometry for motility testing[12-15]. The daisy-chained configuration of the impedance electrodes in the present system differ significantly from other systems[17-19], where the impedance electrode pairs are located far from each other. As shown in previous impedance studies[5,6] this catheter configuration offers a high spatial resolution for detailed monitoring of bolus transport patterns. The incorporated solid state pressure transducers allow the concurrent analysis of the corresponding contractile events.

As shown in Figure 3, the phase 3 complex is recorded identically by both techniques, showing the well-known characteristics of the migrating motor complex, similar to recent findings by Imam *et al*[17]. During the postprandial phase, chyme transport and associated peristaltic activity can be accurately monitored, and thus a large number of bolus transport event (BTE) was obtained for detailed analysis.

Considering the manometry tracings alone, it has been

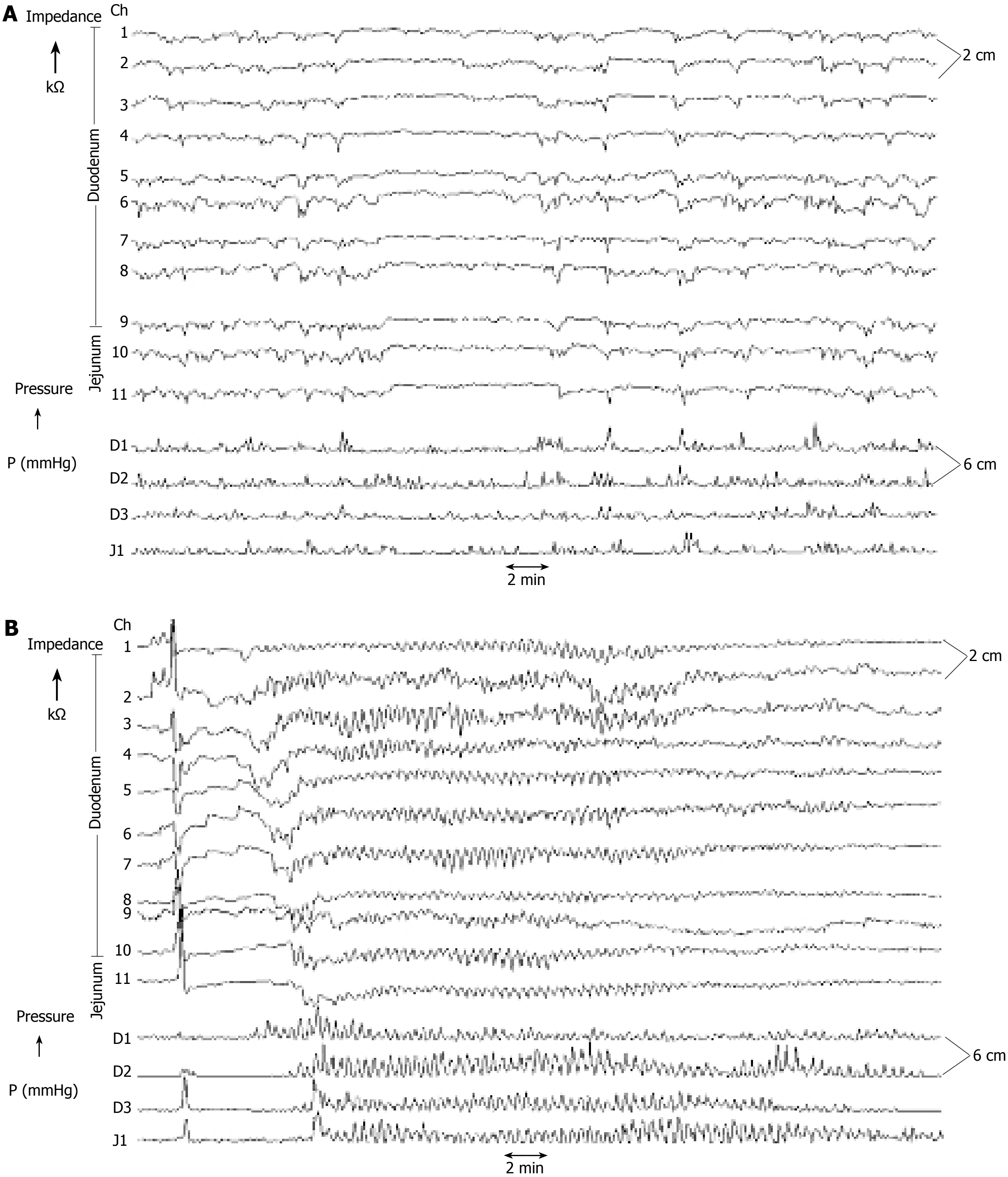

Figure 3 Concurrent Impedance Manometry (CIM) tracings. Upper panel: During the interdigestive phase irregular chyme transport at the impedance channels and irregular motor activities at the pressure channels are observed. Lower panel: A phase 3 complex displays nearly identical features with frequent changes of both pressure and impedance.

shown to be difficult to characterize contraction waves to be stationary or propagated[20]. As shown in Figure 4 this problem can be overcome by the combined technique as shown in the recent study. After a bolus transport event (BTE) had been identified with impedance in the present study, the organization of the associated contraction waves could be analyzed. We did not include contraction waves that occurred between the bolus transport events, as compared to previous studies[1,3,20], which analyzed the overall motility activity. Therefore, the results are not comparable. As only impedance events representing a bolus transport over at least 6 cm were analysed, the present results provide data about the postprandial organization of peristaltic activity in association with a transduodenal bolus transport. Transpyloric chyme movement was not included in the present studies.

A major finding of the present study is the close relationship between transduodenal bolus transport patterns and peristaltic contraction patterns. The results showed that long-spanned chyme transport patterns are predominantly associated with propagated peristaltic patterns, whereas short-spanned chyme transport patterns

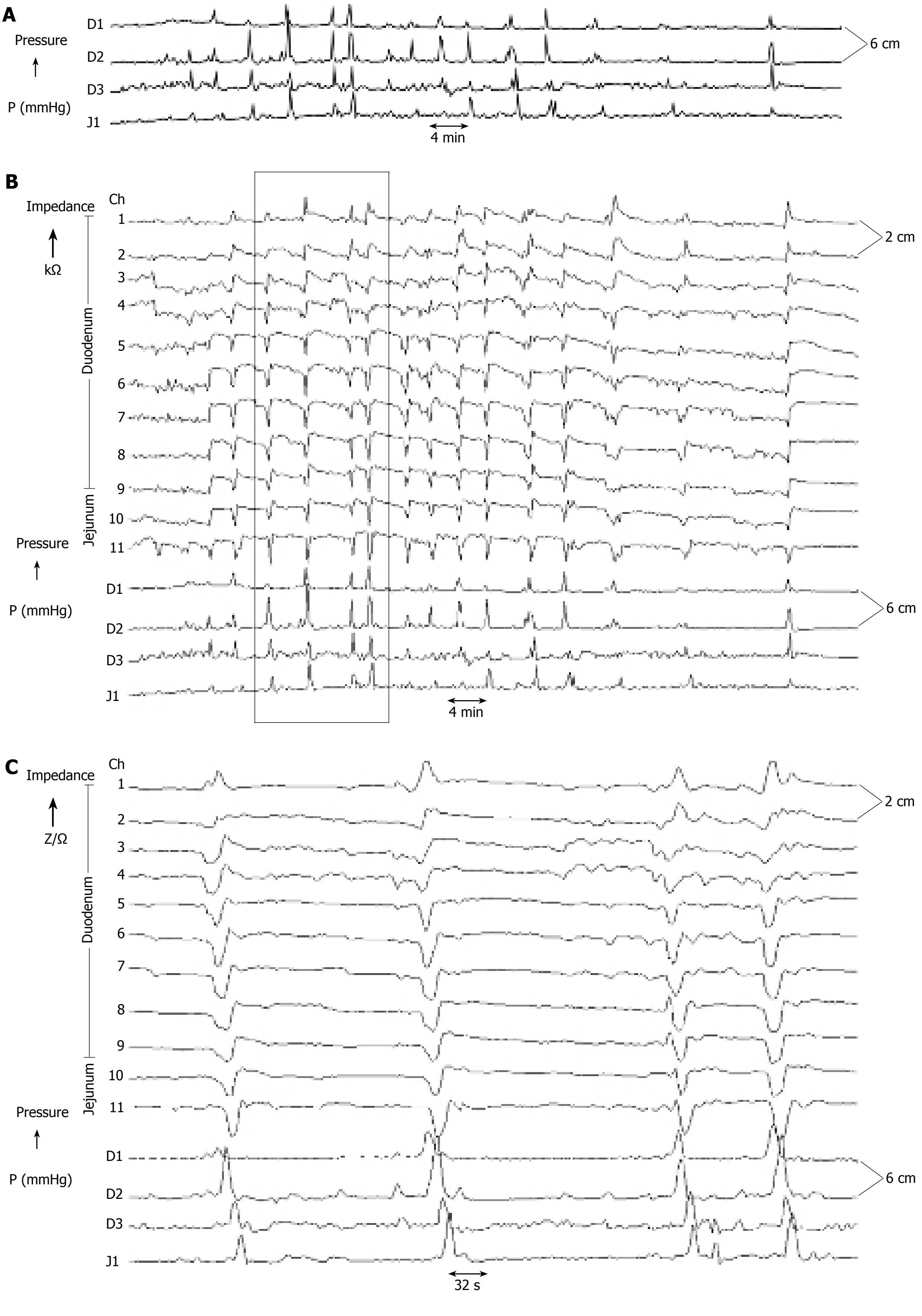

Figure 4 Concurrent Impedance Manometry (CIM) tracings after a test meal. Upper panel: Low time scaled manometry tracings of the postprandial state. Middle panel: Low time scaled impedance manometry tracings of the same period as above showing several bolus transport events with associated peristaltic activities. Lower panel: High time scaled impedance manometry tracings of the box allowing identification and classification of bolus transport patterns as well as analysis of associated peristaltic patterns.

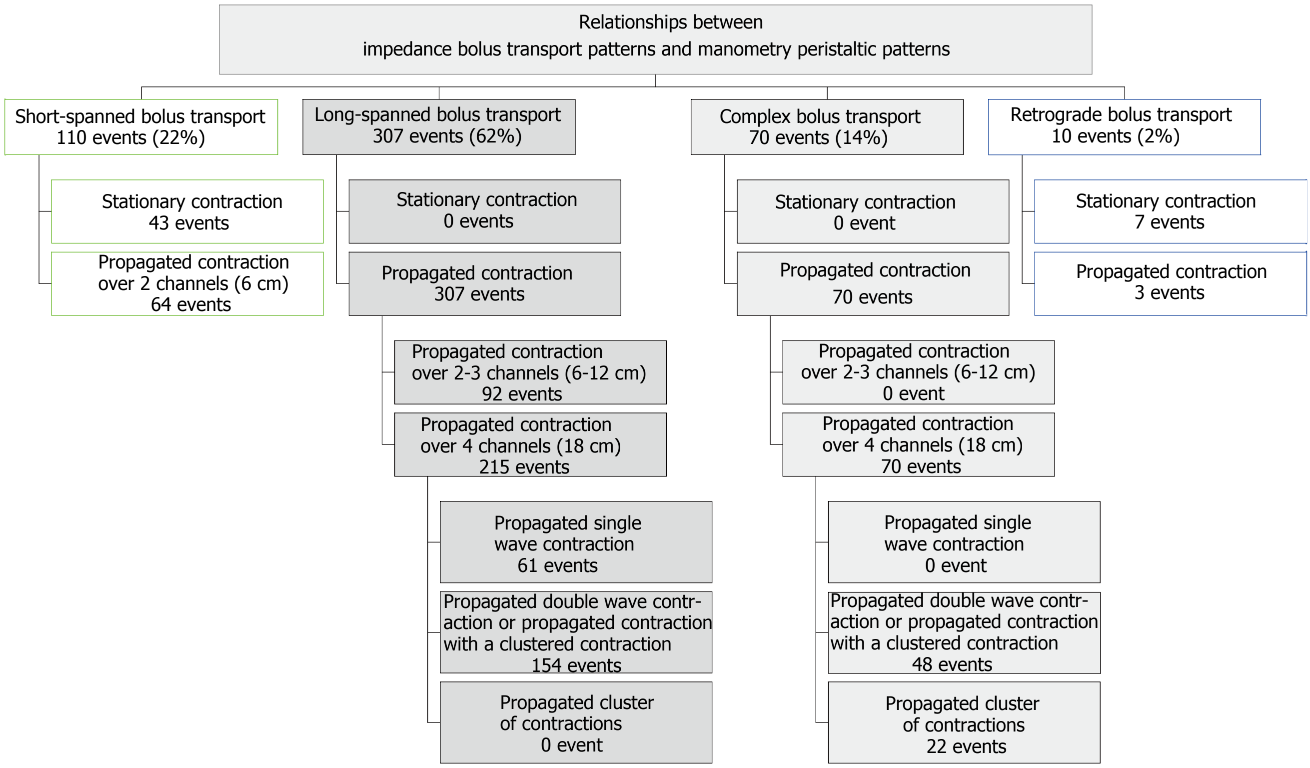

Figure 5 Distribution of bolus transport patterns and associated peristaltic patterns (see text for details).

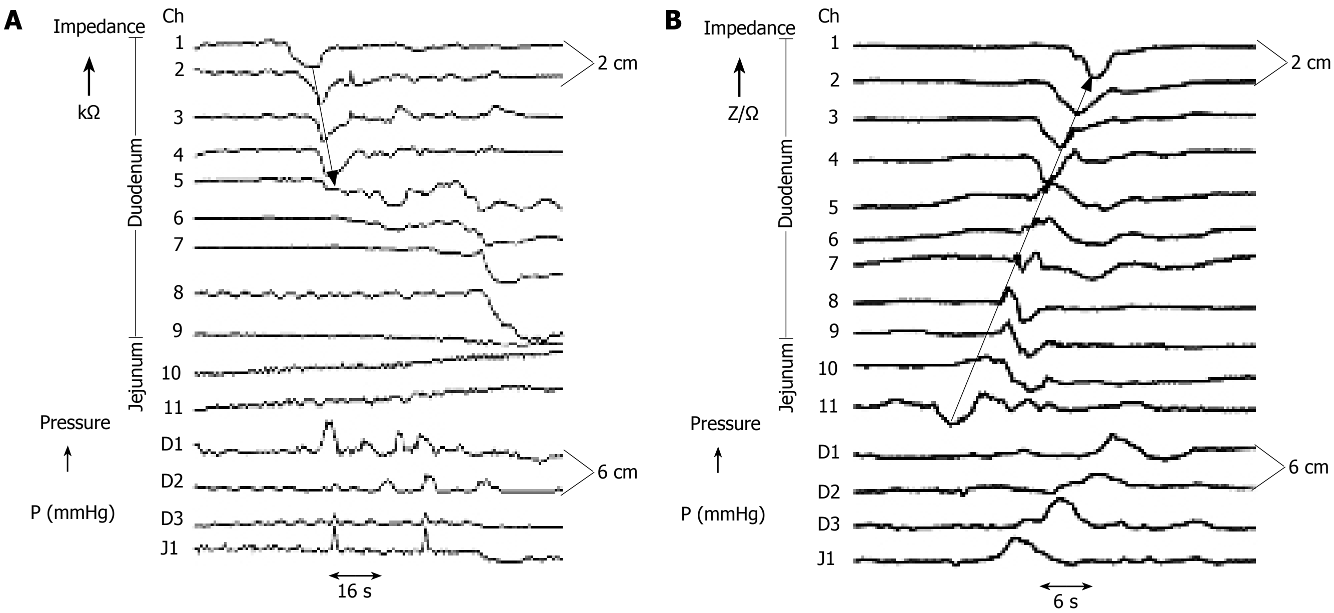

Figure 6 Examples of simple bolus transports and associated peristalsis. Upper panel: Short-spanned bolus transport with associated stationary contraction. Lower panel: Retrograde bolus transport with associated retrograde peristalsis.

are frequently related to stationary contractions or propagated contractions over short distance (6 cm). The data are consistent with results of a recent study[17] showing that impedance corresponds better with fluoroscopic flows than manometry and that recording of pressure events can underestimate even flow events of substantial length. However, the quantitative data of this study are not comparable to ours because there are important differences with respect to study design and analysis algorithm: (a) in this study the impedance segments were spaced 5 cm apart from each other as compared to the cascade configuration in our study, thus, the recording of impedance patterns differs substantially; (b) all impedance events with a drop of 12% or more below baseline, even if detected in only one impedance segment (spread distance < 5 cm), were included as compared to impedance signals of a complete bolus passage over 6 cm in our study. Since an impedance drop only indicates arrival of a bolus front but not always a complete bolus passage, it might represent transpyloric chyme movement into the proximal duodenum, which is

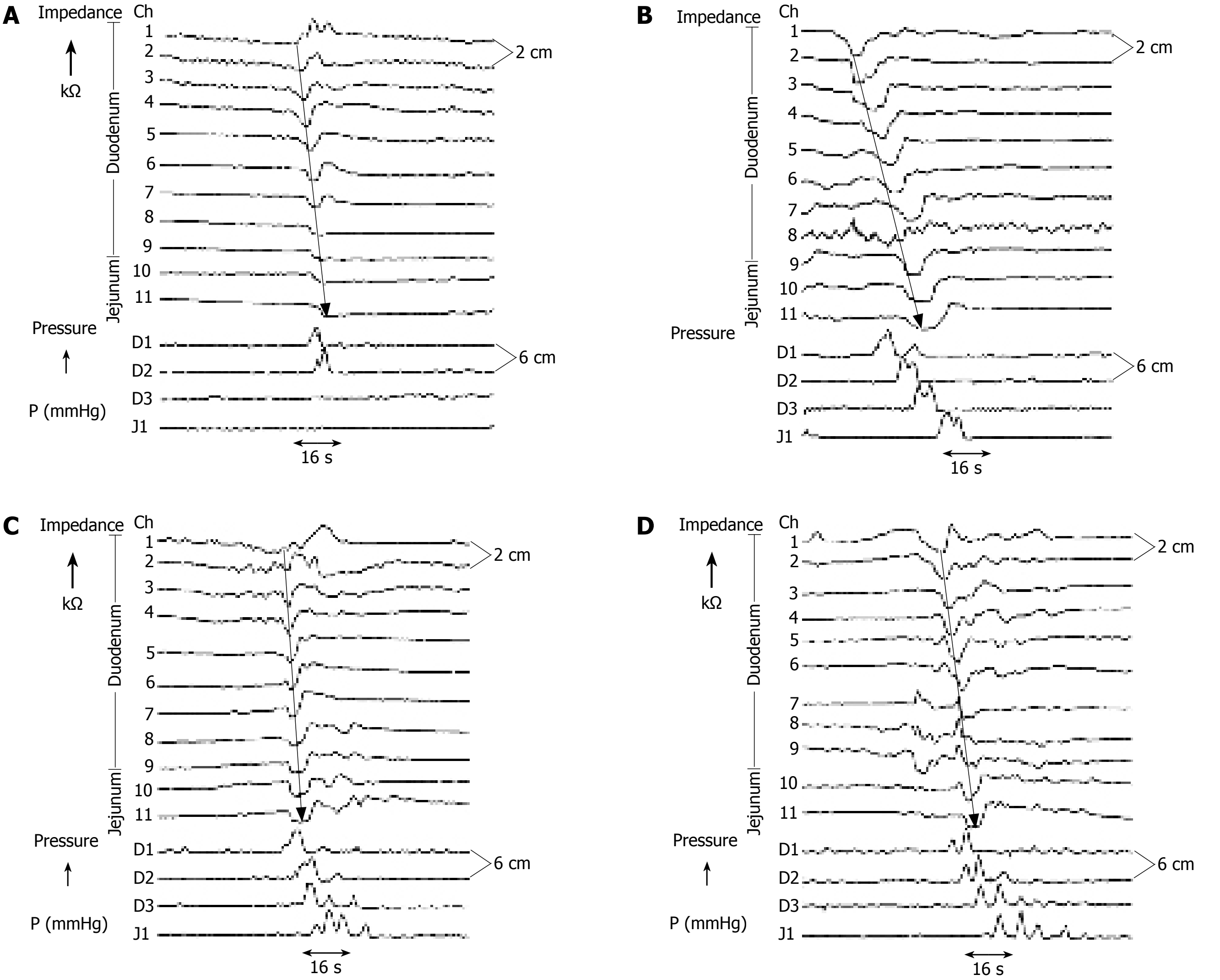

Figure 7 Examples of long-spanned bolus transports and associated peristalsis. (**A**) A long-spanned bolus transport with the bolus front traversing the whole duodenum. The associated peristaltic sequence displayed a propagated single wave contraction from D1 to D2. This peristaltic pattern was classified to be simple (propagated single wave contraction). (**B**) A long-spanned bolus transport traversing the whole duodenum. The associated peristaltic sequence displayed a propagated contraction with a double wave contraction at channel D1 and double spike contractions at D2, D3 and J1. This peristaltic pattern was classified to be complex (propagated contraction with a double wave contraction). (**C**) A long-spanned bolus transport with the bolus front traversing the whole duodenum. The associated peristaltic sequence displayed single wave contractions at channel D1-D3 and a clustered contractions at J1. This peristaltic pattern was classified to be complex (propagated contraction with a clustered contraction). (**D**) A long-spanned bolus transport with the bolus front traversing the whole duodenum. The associated peristaltic sequence displayed double wave contractions at channel D1 and a clustered contractions at D2, D3 and J1. This peristaltic pattern was classified to be complex (propagated cluster of contractions).

detected at the first duodenal channel as compared to a transduodenal bolus transport over at least 6 cm.

Another major finding is related to the motor mechanisms regulating transduodenal bolus transport. Distinct peristaltic patterns have been identified. Our data showed, that if a bolus is propelled over a long distance (> 4 pressure channels or 18 cm), it is frequently associated with a complex peristaltic sequence, which can be either a propagated contraction with double wave contraction, a propagated contraction with a clustered contraction, or rarely, a propagated cluster of contractions. The finding that cluster of contractions (double wave contraction, clustered contraction) are an integral part of a peristaltic sequence associated with a transduodenal bolus transport is new. The retrospective analysis of these contraction patterns without the associated impedance tracings frequently fails to clearly identify the clustered contractions to be a part of bolus-associated peristaltic sequence. These results may explain the facts that the analysis and classification of all contraction waves in human small intestine is difficult, and most of them have been classified to be stationary[20].

The dominant patterns of propulsive bolus transports with associated propulsive peristaltic patterns support the existence of a precise spatial and temporal organization of the contraction waves in human duodenum during the postprandial state[21-24]. Two recent studies investigating the relationships between antral contraction, transpyloric fluid flow and duodenal motility observed that transpyloric fluid transport is associated with duodenal propagation[18,21]. The results of the present study strongly support previous reports showing that coordinated duodenal contraction waves are an important determinant regulating antroduodenal chyme flow[22,24,25], as well as gastric emptying[26].

The recent finding of different propulsive bolus transport patterns associated with different propulsive

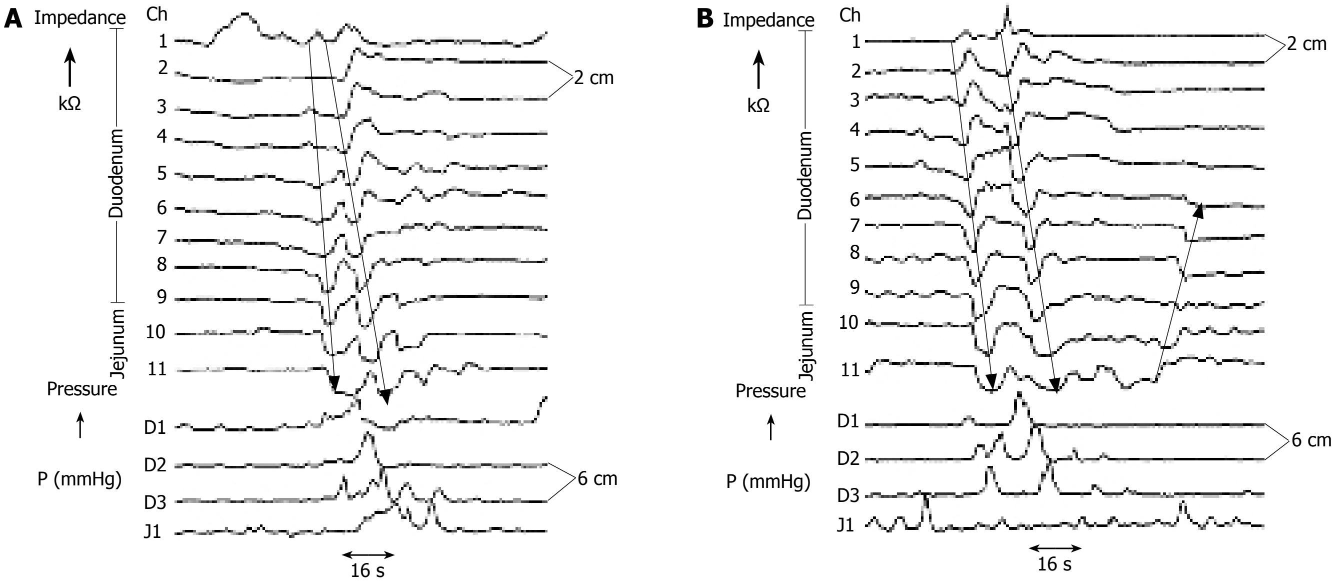

Figure 8 Examples of complex bolus transports and associated complex peristalsis. (**A**) A complex bolus transport with two components propelling with different propulsion velocity as illustrating by the arrows. The associated peristaltic sequence is complex showing a long lasting double spike contraction at D1, a single wave contraction at D2, a clustered contraction at D3 and a multispike double wave contraction at J1. (**B**) A complex bolus transport comprising two boluses following each other very rapidly as illustrating by the anterograde arrows. The associated peristalsis showed two separate peristaltic sequences which seemed to be connected together by a interpolate contraction wave at D2. A retrograde bolus movement (retrograde arrow) seemed to be derive from a retrograde peristaltic sequence with a single contraction wave seen at J1.

peristaltic patterns underlines the physiological difference between the duodenum and the esophagus, where the bolus transport patterns are highly uniform and the peristaltic sequences are predominantly simple[7,13]. This finding support the view that the duodenum is not only a conduit but also an active segment, which is able to generate contractions transporting and mixing gastric contents together with duodenal juices into the jejunum[27-31]. Since previous studies[32,33] indicated that contraction patterns in the duodenum are quite different from those in the jejunum, further studies should examine, if similar bolus transport patterns and peristaltic patterns will be found in other segments of the gut.

The answers about the question regarding how complex peristaltic sequences can be regenerated during a bolus transport can be sought in results of electrophysiological studies. Intestinal motility is considered to be controlled by interaction between myogenic, neural and humoral factors[34-35]. In recent studies several motility patterns have been characterized as peristaltic or pendular, stationary or propagating, or twitch or segmental[36-37]. Furthermore, several electrical signals have been shown to be associated with different types of contractions including slow waves, spikes, or bursts[36-38]. Therefore, peristalsis with associated propagated peristaltic waves should not be regarded as a simplex reflex, bur rather as a co-ordinated locomotor pattern, which can be induced either by fluid distension, local stretch, or mucosal stroking[36]. Careful examination of the spatial and temporal relationship between spontaneous slow waves and peristaltic waves showed that they seem to constitute two separate electrical events that may drive two different mechanisms of contractions[39]. Slow waves are not in rhythm with peristaltic waves and they may occur in different groupings and patterns. These waves may travel in the same or in opposite directions from each other and may propagate in the oral or caudal direction, and therefore, may modulate each other. Similarly, slow waves and spikes seem to be propagated by different mechanisms through different cell networks[32]. Thus, the spatial and temporal characteristics of contraction in the small intestine seem to be determined not only by the direction of the slow wave but also whether or not spikes are generated after these slow waves[32,40].

There are 2 limitations of the recent studies, which should be evaluated in further studies: (a) since the composition of the test meals significantly affect small intestine motility, it remains to be determined, if the recent bolus transport and peristaltic patterns will be the same by using different test meals; (b) since the intertransducer distance significantly affect the recognition of propagated pressure waves, it remains to be determined, if more closely spaced recording points with 1-2 cm apart may provide more accurate data.

In summary, combined impedancometry and manometry in human duodenum provides detailed data about the relationship between the organization of contraction waves and the patterns of chyme flow during the postprandial state. This technique improves the analysis of intestinal motility. Several postprandial peristaltic patterns associated with transduodenal bolus transport have been identified showing that cluster of contractions constitutes an integral part of the peristaltic sequence associated with transduodenal bolus transport. The results provide new insights into the peristaltic mechanisms that are associated with transduodenal chyme transport and maintain the physiological function of the duodenum. The present results clearly indicate that comprehensive motility testing in the small intestine, particularly during the postprandial state, should be performed using the combined technique. The present data will serve as basis findings forwarding clarifying small intestinal motor dysfunction.

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