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REVIEW

Technological insights: Combined impedance manometry for esophageal motility testing-current results and further implications

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Abstract

This review focuses on current aspects of the novel technology of combined impedance manometry for esophageal motility testing. It presents methodological features, summarizes current results and discusses implications for further research. The combined technique assesses simultaneously bolus transport and associated peristalsis, thus allowing detailed analysis of the relationships between bolus transit and esophageal motility. Recent studies demonstrate that combined impedance manometry provides important additional information about esophageal motility as compared to conventional manometry: (1) monitoring of bolus transport patterns, (2) calculation of bolus transit parameters, (3) evaluation of bolus clearance, (4) monitoring of swallow associated events such as air movement and reflux, and (5) investigation of the relationships between bolus transit and LES relaxation. Studies with healthy subjects have identified several useful parameters for comprehensive assessment of eosphageal function. These parameters were found to be pathological in patients with classical achalasia, mild GERD, and ineffective esophageal motility. The technology of combined impedance manometry provides an important new tool for esophageal function testing, advancing both clinical and basic research. However, several important issues remain to be standardized to make the technique suitable for widely clinical use.

Key words: Combined impedance manometry; Esophageal function testing; Review

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INTRODUCTION

The basic function of the esophagus is the transport of the bolus from the pharynx into the stomach. Esophageal peristalsis is based on propulsive mechanisms along the axis of the organ, generated by a latency gradient that is modulated by the inhibitory neurotransmitter nitric oxide[1-3]. Much is known about the physiological and pathological phenomena of peristalsis based on intraluminal manometry[4], and up to now, this technique is the standard method to study esophageal motility[5-7]. But until recently, the relationships between peristalsis, intrabolus forces and bolus transport could be assessed by radiological contrast studies only[8-10]. For this purpose, other technologies have emerged, such as ultrafast computed tomography[11,12], intraluminal high frequency esophageal ultrasonography[13], and topographical esophageal manometric methods[14]. However, these techniques are expensive, require specific technical support and personal expertise, and do not clarify some details of bolus transport along the esophagus.

In 1991, Silny described a new catheter-related procedure for high-resolution measurements of gastrointestinal motility and bolus transport based on intraluminal measurements of electrical impedance[15]. Subsequently, this technique was validated by means of manometry and videofluoroscopy studies[16-18] and it was applied for studying of intestinal chyme transport[19,20], for monitoring of reflux[21-23], and for evaluation of esophageal bolus transport[24].

However, the impedance technique alone also has some limitations. The contraction amplitude, an important parameter in predicting organ function, cannot be determined[25]. Impedance measurements without manometry can underestimate some aspects of the relationships between esophageal wall movement and bolus motion, especially in patients with dysphagia or chest pain. In order to cope with these difficulties, a second generation of impedance catheters was developed[26]. The catheter integrates impedance monitoring and manometry

in a single device. Thus, both tests can be performed simultaneously and the relationships between the dynamics of bolus transport and wall motion can be analysed well, while the quality of recording is maintained.

Recently combined impedance manometry has been increasingly applied for esophageal motility testing[27-36]. This report summarizes current results and discusses future prospects of this novel technique.

SCIENTIFIC BASICS

The method is based on the esophageal intraluminal measurement of electrical impedance and pressure between a number of arranged impedance electrodes and pressure sensors during a bolus passage using an intraluminal probe (Figure 1).

The intraluminal electrical impedance is inversely proportional to the electrical conductivity of the luminal contents and the cross-sectional area (Figure 1). Compared to the muscular wall, air has a lower electrical conductivity and yields increased impedance. In contrast, saliva or nutrients show a higher conductivity and therefore cause an impedance drop at the corresponding measurement segments. On the other hand, luminal dilatation results in an impedance drop, whereas luminal narrowing causes an increase in impedance[15].

The bolus passage along each measured segment allows the delineation of the typical tracing of impedance, which includes a maximum of five phases (Figure 2, upper panel): (1) phase 1 is the resting stage of the organ; (2) phase 2 represents the facultative arrival and passage of an air volume ahead of the bolus; (3) phase 3 is associated with the arrival and the passage of a bolus. The initial rapid fall of impedance is associated with the arrival of the bolus front as bolus entry (F-Point). During the subsequent nearly plateau phase the bolus is mainly located within the measuring segment; the minimum impedance during this phase represents the bolus body (B-Point); (4) during phase 4 the bolus leaves the measuring segment as bolus exit due to wall contraction with facultative lumen occlusion, which can be represented by the maximum impedance (C-Point); (5) phase 5 is the transitory stage to resting stage. This characteristic impedance wave form may change in the case of absence of air in front of the bolus or absence of a lumen-occluding contraction wave (Figure 2, upper panel). For visualization of the maximum and minimum impedance values an individual scaling (Figure 2, lower panel, left side) can be used instead of the standard scaling (Figure 2, lower panel, right side).

The F-Point, B-Point and C-Point can be determined by computer assistance according to the presumed definitions, as shown in Figure 3, left panel. Alternatively, bolus entry and exit have been defined as follows[33,34]: Bolus entry is considered to occur at the 50% point between impedance baseline and impedance nadir during bolus passage, and bolus exit is determined as 50% point on the impedance recovery curve, as shown in Figure 3, right panel.

EQUIPMENT AND TECHNOLOGY

There are two prototypes of combined impedance manometry catheters available (Figure 4)

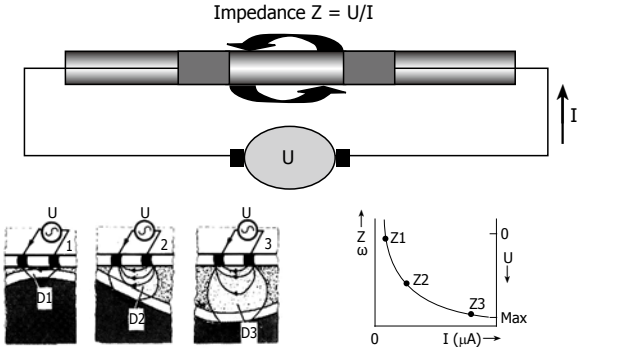

Figure 1 Upper panel: Principles of intraluminal impedancometry: the electrical impedance (Z) of a electric field between 2 electrodes is the ratio between applied voltage (U) and resulting current (I). Lower panel: Impedance is non-linearly inversely dependent on bolus diameter and electrical conductivity of luminal content.

(1) 15-channel esophageal function testing catheter[26-30]: the impedance-manometry catheter is a polyvinyl catheter with an external diameter of 2.5 mm. The catheter consists of 11 impedance segments (each 2 cm long) and 4 semiconductor solid-state pressure transducers to register the manometry tracings. The solid-state pressure transducers are located at the junction between the impedance channels 1-2, 4-5, 7-8, and 10-11, with an intertransducer distance of 6 cm (Figure 4, left panel). (2) 9-channel esophageal function testing catheter[31-35]: it incorporates five pressure (two circumferential and three unidirectional) sensors and four impedance-measuring segments. The two circumferential solid-state pressure sensors are located at 5 cm and 10 cm from the tip and three unidirectional pressure sensors at 15, 20, and 25 cm. Impedance measuring-segments consist of pairs of metal rings placed 2 cm apart, centered at 10, 15, 20 and 25 cm from the tip, thus spanning the four proximal pressures transducers (Figure 4, right panel).

The first system[26-30] displays a cascade configuration of the impedance measuring segments similar to the systems used in previous impedance studies for the study of bolus transport[19,20,24] and for monitoring of reflux[21,22]. The pressure transducers also serve as impedance electrodes and are located exactly at the junction between 2 adjacent impedance segments (the end of one segment and beginning of the adjacent segment). In contrast, in the other system[31-35] the impedance segments are arranged at an intersegmental distance of approximate 2 cm. Furthermore, the pressure transducers are located inside the impedance segment.

STUDY PROTOCOLS

The procedure is very similarly to standard manometry. The patients are asked to fast for at least 8 h before recording. In the sitting position, the recording assembly is passed nasally and positioned with all sensors in the stomach. The intragastric pressure is set as baseline pressure. With the subject lying in the supine position and after a 10-min accommodation period, a station pull-through is performed to accurately locate the LES

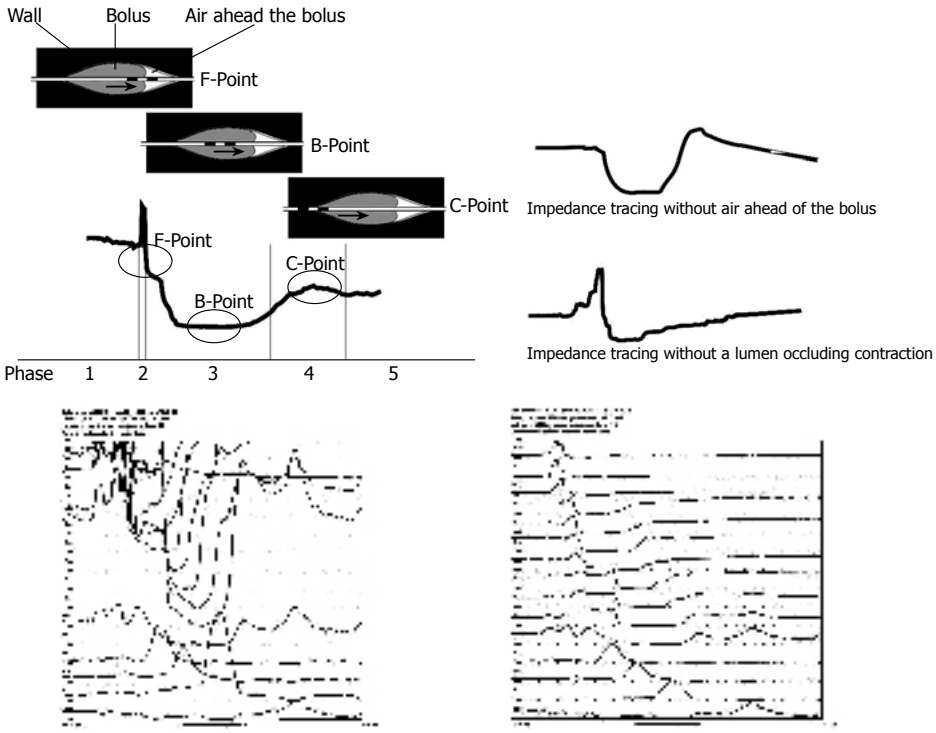

Figure 2 Upper panel: Characteristics of the impedance tracing during bolus passage in the esophagus of healthy persons. The black electrodes indicate a measuring segment. From baseline, the initial sudden impedance increase represents the arrival of ingested air ahead of the bolus. During the rapid impedance fall due to the arrival of the bolus, the bolus head (F-Point) can be determined as the return of impedance closely to baseline. The bolus passage is represented by a further decrease of impedance followed by a plateau phase. During the plateau phase (phase 3) the bolus is located within the measuring segment. The minimum impedance value during this phase is related to the maximum bolus volume located within the segment, which represents the bolus body (B-Point). Subsequently impedance increases due to wall contraction and the bolus is leaving the segment. The maximum value during impedance increase back to baseline is associated with the moment of lumen occlusion (C-Point). Dependent on bolus volumen and bolus viscosity the exact position of the points of interest is variable as indicated by the oval circle. The impedance tracing may be variable as shown at the right side without air ahead of the bolus or without a rapid lumen occluding contraction. Lower panel: For visuallisation of the minimum and maximum impedance an individual scaling (left side) can be used instead of a normal scaling (right side).

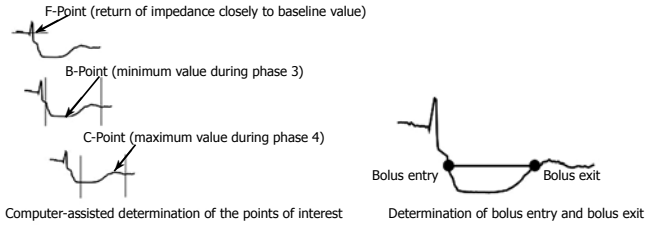

Figure 3 Upper panel: computer assisted determination of the points of interest according to presumed definitions as suggested by Nguyen *et al*[24,27,29]. Lower panel: bolus entry and bolus exit can be considered to be 50% of the basal impedance as compared to nadir impedance as suggested by Tutuian *et al*[32,33,34].

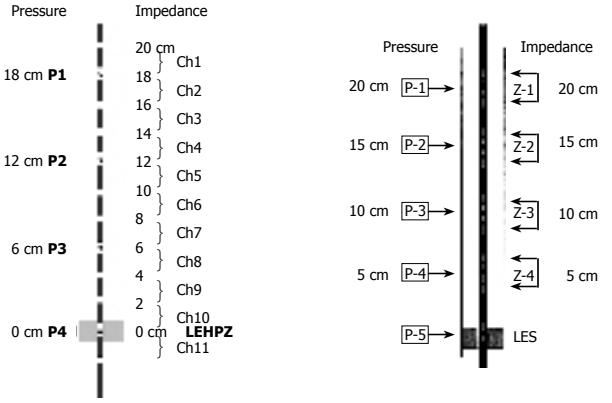

Figure 4 The 2 recently available systems of combined impedance manometry. During esophageal motility testing the most distaly located pressure transducer was positioned at the lower esophageal high pressure zone. Left panel: 15 channel catheter for combined impedance-manometry procedure. The 4 semiconductor solid-state pressure transducers (P1-P4) serve also as impedance electrodes and are placed at 6 cm distance each. There are 11 impedance segments, each 2 cm long (Ch1-Ch11) with a cascade configuration. The solid-state pressure transducers (P1-P4) are located exactly between the impedance channels 1-2, 4-5, 7-8 and 10-11, respectively. Right panel: 9-channel esophageal function testing catheter with five pressure sensors and four impedance-measuring segment. The impedance measuring-segments consist of pairs of metal rings placed 2 cm apart, centered at 10, 15, 20 and 25 cm from the tip (Z1-Z4). Four of five the pressure sensors are located within the impedance segments (P1-P4). The 5th pressure sensors (P5) is located 5 cm from the tip.

position. The most distal pressure sensor is placed at the level of the LES at the point at which the highest sphincter pressure is obtained during the pull-through procedure, the so-called lower esophageal high-pressure zone (LEHPZ).

To evaluate esophageal peristalsis and its associated bolus transport, liquid boluses (5 mL or 10 mL physiological saline) and semisolid boluses (5 mL standard viscous material provided by Sandhill Scientific Inc. or 10 mL of a commercially available plain yogurt, Morbo, Borken, Germany) are administered. The boluses are dispensed into the mouth with a syringe and the swallows are performed on command. All swallows are separated by at least 30 s during which no esophageal peristaltic occurs. An event marker is used to denote each swallow event. When a second swallow is incidentally initiated within 20 s of the primary event, both swallows are excluded from analysis. For each investigation, the baseline impedance is determined as the first predeglutitive impedance. After each yogurt bolus, at least 2 swallows of water are administered to clear small amounts of bolus material attached to the probe, until the impedance returns closely to baseline ($\leqslant$ 5% deviation).

PHYSIOLOGICAL OBSERVATIONS

With combined impedance manometry 3 different features of bolus transport can be obtained during swallowing (Figure 5): (1) monitoring of bolus transport patterns, (2) calculation of bolus transport parameters, and (3) monitoring of swallow associated events. These features can not be obtained by conventional techniques such as manometry or fluoroscopy.

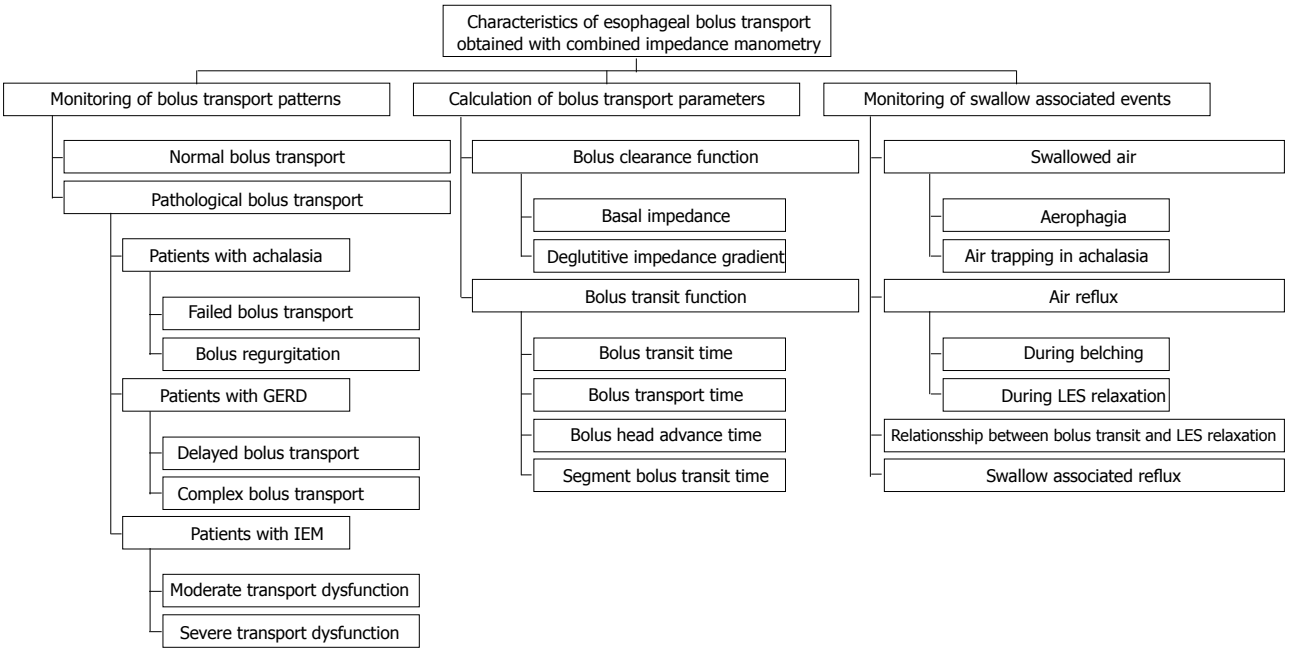

Figure 5 Characteristics of bolus transport as obtained by combined impedance manometry.

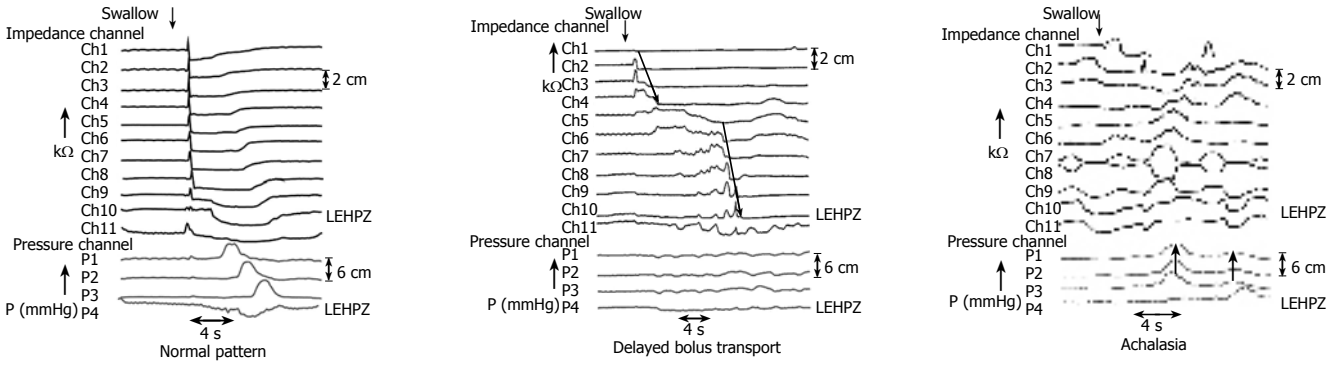

Figure 6 Bolus transport patterns as obtained by combined impedance manometry normal pattern (left panel), delayed bolus transport (middle panel) in some patients with GERD, failed transport (right panel) in patients with achalasia.

Monitoring of esophageal bolus transport patterns (Figure 6)

Recent results indicate that monitoring of bolus transport patterns may be helpful for the characterization of pathological esophageal bolus transport. (1) Healthy subjects show characteristic impedance patterns of continuous bolus transit through the esophagus into the stomach; (2) In patients with achalasia the manometry patterns are unique, while the impedance patterns are very variable[28]. Different pathological patterns of bolus transport have been observed in patients with achalasia. They are (a) failed swallow-induced bolus transport through the esophagus in all cases, and (b) impedance evidence of luminal content regurgitation together with excessive air trapping. The results may explain some symptoms in achalasia, including chest pain and regurgitation; (3) In patients with GERD several pathological bolus transport patterns types have been described[29], including failed bolus transport, delayed bolus transport, and complex bolus transport. The contribution of these phenomena and the clinical significance regarding to dysphagia symptoms remains to be determined.

Calculation of bolus transport parameters (Figure 7)

(1) Baseline impedance: It has been shown that there is a significant difference between gastric and esophageal baseline impedance in healthy subjects[27] and a significant difference of esophageal baseline impedance between healthy subjects and achalasia patients[28]. The results indicate that this parameter may be used to describe the esophageal resting state, including lumen width and filling state, particularly in minimal disease states. (2) Deglutitive impedance gradient: It has been shown that the postdeglutitive impedance is significantly lower in GERD patients as compared to healthy subjects, indicating that the deglutitive impedance gradient can be used to assess the propulsive esophageal clearance function[29]. For correct calculation of this parameter, repetitive clearing swallows between test swallows are necessary[29]. This parameter should be evaluated and standardized in further studies to determine its clinical significance for the definition of complete bolus transit. (3) Parameters of bolus transport: Several parameters can be calculated during impedance studies, i.e. propulsion velocity or transit time of bolus,

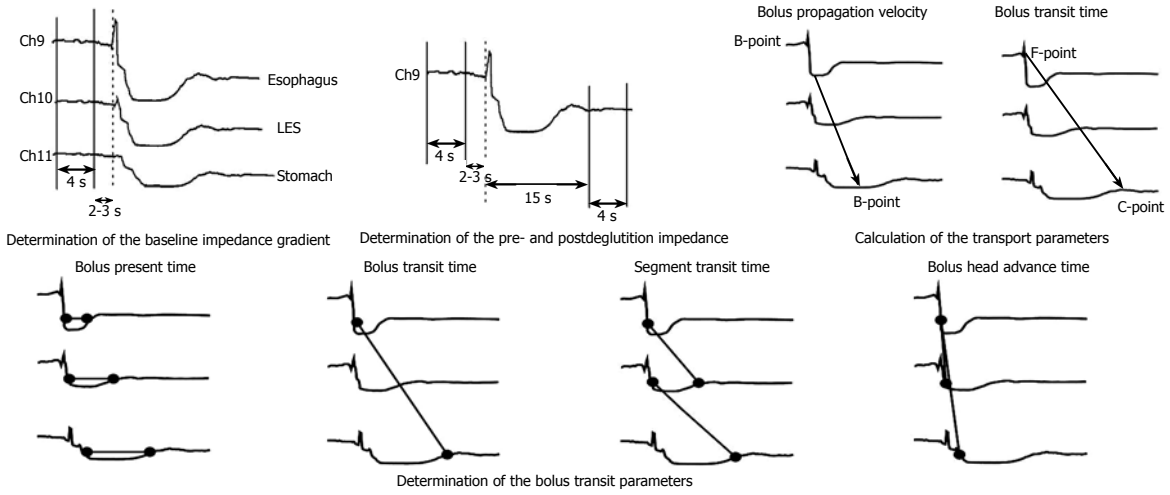

Figure 7 Bolus transport parameters, which can be obtained by combined impedance manometry according to presume definitions of the points of interest.

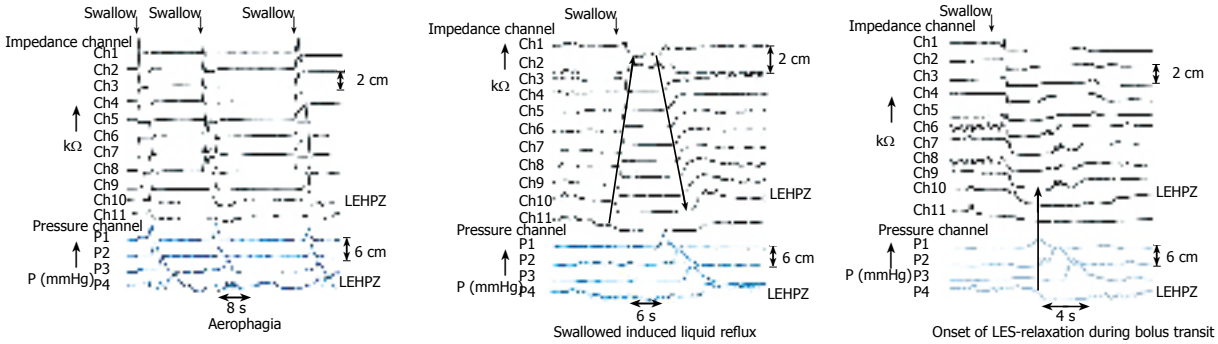

Figure 8 Swallow associated events as obtained by combined impedance manometry areophagia (left panel), swallow induced reflux (middle pannel), relaxationship between bolus transit and LES-Relaxation (right panel).

bolus head and bolus tail[24,27,29] or total bolus passage time, bolus head advance time, bolus presence time, and bolus transit time[32-34]. The dynamics of the bolus transport along the esophagus has been described in detail[24]. These parameters clearly discriminate liquid from semisolid boluses and show that bolus transport depends on both test substance and body position[24,31,32]. (4) Quantitative data in healthy subjects indicate that impedance and manometry provide independent parameters of esophageal motor function[27,33]. There is no clear correlation between contraction amplitude and bolus propagation velocity[27]. As normal esophageal volume clearance may occur within a wide range of peristaltic amplitudes[8], it is possible that after a critical pressure, excess amplitude does not appear to be needed to move the bolus. (5) Quantitative data in patients with mild GERD demonstrate delayed bolus transit in patients with non-erosive GERD and GERD grade I, indicating that combined impedance-manometry may increase the sensitivity for detection of minor motility abnormalities[29]. (6) Quantitative data in patients with ineffective esophageal motility[34] indicate that presumed "ineffective" low-amplitude esophageal peristaltic contractions of < 30 mmHg[37] may be associated with a substantial number of complete transit: 23 patients (3.9%) had normal bolus transit for both liquid and viscous swallows, 12 patients (17.1%) had normal bolus transit for liquid swallows and abnormal bolus transit for viscous swallows, and 10 patients (14.3%) had normal bolus transit for viscous swallows and abnormal bolus transit for liquid, whereas 25 patients (35.7%) had abnormal bolus transit for both liquid and viscous. The results indicate that combined impedance manometry better describes and classifies patients with ineffective esophageal motility according to severity: no functional abnormalities with normal transit, moderate functional abnormalities with abnormal transit either for liquid or viscous boluses, and severe functional abnormalities with abnormal bolus transit for both liquid and viscous boluses.

Monitoring of swallow-associated events (Figure 8)

(1) Movement of air during swallowing: In early studies it was shown that one advantage of the impedance technique is the monitoring of air movement during swallow and LES-relaxation[24]. Recent studies have expanded the finding of esophageal air movement in patients with achalasia, so-called air trapping[28], as well as during aerophagia[36]. The clinical significance of this phenomenon as a cause of dysphagia remains to be determined. (2) Swallow-associated reflux: Different types of reflux have been observed in patients with GERD during swallowing[29]: (a) liquid reflux initiated by a swallow and preceding the regular bolus transport, (b) liquid reflux

following a swallow-induced regular bolus transport, and (c) spontaneous liquid reflux initiating a clearing swallow. Since conventional 24-h pH-monitoring does not differentiate between fasting and deglutition associated reflux, the prevalence of these impedance phenomena and their relevance for mucosal damage have yet to be defined. (3) Relationships between bolus transit and LES relaxation: Our recent study[30] revealed close relationships between bolus transit and LES relaxation. In 76% of the cases LES relaxation occurs during bolus transit, when the position of the bolus is very close to the LES. The results indicated that LES-relaxation may be partially initiated by bolus transit. The clinical significance of this finding for characterization of patients with LES-dysfunction other than achalasia - such as hypertensive LES or poorly relaxing LES - should be evaluated. Using high-resolution impedance monitoring, the opening patterns of the esophageal gastric junction during deglutition and transient lower sphincter relaxation have been studied recently[37].

CLINICAL RELEVANCE

Clinical studies showed that combined impedance manometry is particularly suitable for comprehensive eosphageal motility testing and monitoring of bolus transport patterns. With impedance different aspects of bolus transport can be obtained: (1) normal and pathological bolus transport patterns including bolus escape and retrograde bolus transport can be monitored, (2) several parameters of bolus transit can be calculated allowing differentiation between normal and abnormal bolus transport, (3) parameters related to bolus propulsive clearance and bolus transit completion can be determined, (4) swallow-associated events such as normal and pathological air movement as well as pathological reflux can be monitored, and (5) the relationship between bolus transit and LES relaxation can be investigated. Thus, using combined impedance manometry complete data about esophageal motor function and associated bolus transport can be obtained during a single investigation. In patients with achalasia the technique provides additional information about the functional status and may explain some symptoms in these patients. However, the gold standard for diagnosis of achalasia remains manometry due the clear definitions and the unique manometry patterns. In patients with GERD combined impedance manometry provides additional information about mechanisms related to disturbed bolus transit and bolus clearance. In patients with ineffective esophageal motility it helps clarifying the associated functional abnormalities. Thus, combined impedance manometry is on the way to be an important tool for obtaining detailed information about the physiology and pathophysiology of esophageal motility. The potential clinical implications of this technique include (1) the functional classification of esophageal motor disturbances in patients with non-obstructive dysphagia; (2) the perioperative management of laparoscopic fundoplication and other (endoscopic) antireflux procedures and (3) the evaluation of pharmacological approaches to esophageal motility and bolus transport.

FUTURE PROSPECTS

However, the studies also indicate that standardization of experimental set-up including equipment, study protocols, and particularly analysis algorithms with definition of the events of interest are important to make the data reproducible and the interpretation of the results more concise. There are important issues to be solved in order to make the technique more reliable and suitable for routine clinical use.

The equipment, particularly the spatial arrangement of impedance segments and pressure transducers should be clarified, because this is the most important determinant for the analysis of the relationship between manometric and impedance events during simultaneous monitoring. Since bipolar impedance measurements are performed between two electrodes, the impedance values obtained are the results of an integrative change of intraluminal electrical conductivity and cross-sectional area in the whole 2 cm segment. This should be kept in mind as an important aspect that differs from point manometry. At each corresponding impedance segment there is a 2 cm distance between the bolus entry point (first electrode) and the bolus exit point (second electrode). In case that the pressure transducer is located at the end of an impedance segment[27,29,30], the impedance and manometric timing of bolus exit are approximately identical. If the pressure transducer is located inside the impedance segments[33-35], the manometry bolus tail is not identical with the impedance bolus tail, as the bolus has not yet left the segment. The appropriate number of impedance segments is another issue. With both available systems several parameters of bolus transport can be obtained. The 15-channel system allows a detailed monitoring of bolus transport patterns and associated events[24,27-30]. It remains to be determined, if these features are clinically significant. In contrast, the 9-channel system allows a significant reduction of data acquisition and reduces production costs, thus it is now available for routine clinical use[31-34].

The analysis algorithm including the definition of bolus entry and bolus exit points should be refined. Since impedance is non-linearly dependent on different parameters around the electrodes such as lumen width and electrical conductivity of luminal contents, the interpretation of impedance tracings is based on impedance changes from variable levels and not from fixed calibrated points: (1) relative impedance changes as compared to baseline or extreme values (maximum and minimum) should be used in favour of absolute values as normally seen in manometry; (2) a small amount of a highly conductive substance may yield the same impedance change as a great amount of a low conductive substance, particularly if the conductivity of luminal contents is highly variable, i.e. gastric contents during reflux or duodenal contents during gastric emptying[38,39], or when different test substances are employed[27,29,33,34].

In the early studies[24,27,29] the points of interests were determined visually with computer assistance according to a presumed definition of these points based on theoretical considerations and small validation studies[15,16]. The analysis is time consuming and therefore not appropriate

for large routine studies. In later studies[33,34], bolus entry is considered to occur at the 50% point between impedance baseline and impedance nadir during bolus passage, and bolus exit is determined as 50% point on the impedance recovery curve. This analysis algorithm is simplified and computerized calculation is possible. However, these conventions may have to be refined. Since the same level of impedance was used both for the bolus head (bolus entry) and the bolus tail (bolus exit), and both for liquid and viscous boluses, this definition implied that bolus geometry remains constant independent from bolus characteristics and that the forms of bolus head and tail are identical, or that the bolus is symmetric, respectively. However, fluoroscopic studies[8] have demonstrated that both conditions are not relevant to real life. Considering the impedance tracing during a bolus passage, bolus entry is associated with a very rapid drop of impedance. In this setting, 5%-10% variation in impedance will not yield significant differences regarding the determination of the bolus head. Therefore, this convention appears to be suitable for determination of the bolus entry. In contrast during bolus exit, impedance increases slowly, and 5%-10% variation will result in significant differences regarding the determination of the bolus tail. Therefore, constant impedance levels may not be appropriate to describe bolus transport under various conditions, particularly for the definition of bolus exit as a parameter for completion of bolus transit[33,34]. Further studies are needed to reach consent on this critical issue.

The study protocols should be standardized and include characteristics of the test substances (viscosity and volume) and information on body position, all of which have been identified as determinants of impedance in several studies[24,27,31,32]. Considering the bolus viscosity, a commercially available test substance with constant viscosity and electrical conductivity should be used as standard[33,34]. Considering the test volume, both 5 mL or 10 mL are used[24,27,33,34]. Traditionally, the 5-mL test volume is used to induce an appropriate manometric esophageal response to a swallow. It has been shown that during deglutition different amounts of air are swallowed together with the bolus[12], which may interfere with impedance recording. According to our personal experience, 10 mL seems to be an appropriate volume[15,16], because the larger volume reduces air swallows that might interfere with impedance recording. Since body position affects the impedance of bolus transport[24,32]-which seems to depend on the degree of inclination as a result of the addition of gravity to bolus propulsion-studies may be performed with subjects at supine or recumbent position to eliminate this gravity affect.

More clinical studies are required to prove if combined impedance manometry effectively helps to improve our management of patients with esophageal symptoms, as did manometry in patients with achalasia several decades ago.

REFERENCES

1 **Diamant NE**. Physiology of esophageal motor function. *Gastroenterol Clin North Am* 1989; **18**: 179-194

2 **Sifrim D**, Janssens J, Vantrappen G. A wave of inhibition precedes primary peristaltic contractions in the human esophagus. *Gastroenterology* 1992; **103**: 876-882

3 **Yamato S**, Spechler SJ, Goyal RK. Role of nitric oxide in esophageal peristalsis in the opossum. *Gastroenterology* 1992; **103**: 197- 204

4 **Arndorfer RC**, Stef JJ, Dodds WJ, Linehan JH, Hogan WJ. Improved infusion system for intraluminal esophageal manometry. *Gastroenterology* 1977; **73**: 23-27

5 **Kahrilas PJ**, Clouse RE, Hogan WJ. American Gastroenterological Association technical review on the clinical use of esophageal manometry. *Gastroenterology* 1994; **107**: 1865-1884

6 **Richter JE**. Oesophageal motility disorders. *Lancet* 2001; **358**: 823-828

7 **Spechler SJ**, Castell DO. Classification of oesophageal motility abnormalities. *Gut* 2001; **49**: 145-151

8 **Kahrilas PJ**, Dodds WJ, Hogan WJ. Effect of peristaltic dysfunction on esophageal volume clearance. *Gastroenterology* 1988; **94**: 73-80

9 **Hewson EG**, Ott DJ, Dalton CB, Chen YM, Wu WC, Richter JE. Manometry and radiology. Complementary studies in the assessment of esophageal motility disorders. *Gastroenterology* 1990; **98**: 626-632

10 **Massey BT**, Dodds WJ, Hogan WJ, Brasseur JG, Helm JF. Abnormal esophageal motility. An analysis of concurrent radiographic and manometric findings. *Gastroenterology* 1991; **101**: 344-354

11 **Pouderoux P**, Shi G, Tatum RP, Kahrilas PJ. Esophageal solid bolus transit: studies using concurrent videofluoroscopy and manometry. *Am J Gastroenterol* 1999; **94**: 1457-1463

12 **Pouderoux P**, Ergun GA, Lin S, Kahrilas PJ. Esophageal bolus transit imaged by ultrafast computerized tomography. *Gastroenterology* 1996; **110**: 1422-1428

13 **Miller LS**, Liu JB, Colizzo FP, Ter H, Marzano J, Barbarevech C, Helwig K, Leung L, Goldberg BB, Hedwig K [corrected to Helwig K]. Correlation of high-frequency esophageal ultrasonography and manometry in the study of esophageal motility. *Gastroenterology* 1995; **109**: 832-837

14 **Clouse RE**, Staiano A, Alrakawi A, Haroian L. Application of topographical methods to clinical esophageal manometry. *Am J Gastroenterol* 2000; **95**: 2720-2730

15 **Silny J**. Intraluminal multiple electric impedance procedure for measurement of gastrointestinal motility. *J Gastointest Mot* 1991; **3**: 151-162

16 **Silny J**, Knigge KP, Fass J, Rau G, Matern S, Schumpelick V. Verification of the intraluminal multiple electrical impedance measurement for the recording of gastrointestinal motility. *Neurogastroenterol Mot* 1993: **5**; 107-122

17 **Fass J**, Silny J, Braun J, Heindrichs U, Dreuw B, Schumpelick V, Rau G. Measuring esophageal motility with a new intraluminal impedance device. First clinical results in reflux patients. *Scand J Gastroenterol* 1994; **29**: 693-702

18 **Frieling T**, Hermann S, Kuhlbusch R, Enck P, Silny J, Lübke HJ, Strohmeyer G, Haeussinger D. Comparison between intraluminal multiple electric impedance measurement and manometry in the human oesophagus. *Neurogastroenterol Motil* 1996; **8**: 45-50

19 **Nguyen HN**, Silny J, Wüller S, Marschall HU, Rau G, Matern S. Chyme transport patterns in human duodenum, determined by multiple intraluminal impedancometry. *Am J Physiol* 1995; **268**: G700-G708

20 **Nguyen HN**, Silny J, Wüller S, Marschall HU, Rau G, Matern S. Abnormal postprandial duodenal chyme transport in patients with long standing insulin dependent diabetes mellitus. *Gut* 1997; **41**: 624-631

21 **Skopnik H**, Silny J, Heiber O, Schulz J, Rau G, Heimann G. Gastroesophageal reflux in infants: evaluation of a new intraluminal impedance technique. *J Pediatr Gastroenterol Nutr* 1996; **23**: 591-598

22 **Sifrim D**, Silny J, Holloway RH, Janssens JJ. Patterns of gas and liquid reflux during transient lower oesophageal sphincter relaxation: a study using intraluminal electrical impedance. *Gut* 1999; **44**: 47-54

23 **Sifrim D**, Holloway R, Silny J, Xin Z, Tack J, Lerut A, Janssens J. Acid, nonacid, and gas reflux in patients with gastroesophageal reflux disease during ambulatory 24-hour pH-impedance recordings. *Gastroenterology* 2001; **120**: 1588-1598

24 **Nguyen HN**, Silny J, Albers D, Roeb E, Gartung C, Rau G, Matern S. Dynamics of esophageal bolus transport in healthy subjects studied using multiple intraluminal impedancometry. *Am J Physiol* 1997; **273**: G958-G964

25 **Nguyen HN**, Silny J, Matern S. Multiple intraluminal electrical impedancometry for recording of upper gastrointestinal motility: current results and further implications. *Am J Gastroenterol* 1999; **94**: 306-317

26 **Nguyen HN**, Winograd R, Silny J, Rau G, Matern S. Concurrent manometry and impedancometry for study of esophageal motility [Abstract]. *Gastroenterology* 2000; **118**: A809

27 **Nguyen HN**, Domingues GR, Winograd R, Koppitz P, Lammert F, Silny J, Matern S. Impedance characteristics of normal oesophageal motor function. *Eur J Gastroenterol Hepatol* 2003; **15**: 773-780

28 **Nguyen HN**, Domingues GR, Winograd R, Lammert F, Silny J, Matern S. Impedance characteristics of esophageal motor function in achalasia. *Dis Esophagus* 2004; **17**: 44-50

29 **Domingues GR**, Winograd R, Lemme EM, Lammert F, Silny J, Matern S, Nguyen HN. Characteristics of oesophageal bolus transport in patients with mild oesophagitis. *Eur J Gastroenterol Hepatol* 2005; **17**: 323-332

30 **Nguyen HN**, Domingues GR, Winograd R, Lammert F, Silny J, Matern S. Relationship between bolus transit and LES-relaxation studied with concurrent impedance and manometry. *Hepatogastroenterology* 2006; **53**: 218-223

31 **Srinivasan R**, Vela MF, Katz PO, Tutuian R, Castell JA, Castell DO. Esophageal function testing using multichannel intraluminal impedance. *Am J Physiol Gastrointest Liver Physiol* 2001; **280**: G457-G462

32 **Tutuian R**, Elton JP, Castell DO, Gideon RM, Castell JA, Katz PO. Effects of position on oesophageal function: studies using combined manometry and multichannel intraluminal impedance. *Neurogastroenterol Motil* 2003; **15**: 63-67

33 **Tutuian R**, Vela MF, Balaji NS, Wise JL, Murray JA, Peters JH, Shay SS, Castell DO. Esophageal function testing with combined multichannel intraluminal impedance and manometry: multicenter study in healthy volunteers. *Clin Gastroenterol Hepatol* 2003; **1**: 174-182

34 **Tutuian R**, Castell DO. Clarification of the esophageal function defect in patients with manometric ineffective esophageal motility: studies using combined impedance-manometry. *Clin Gastroenterol Hepatol* 2004; **2**: 230-236

35 **Tutuian R**, Castell DO. Combined multichannel intraluminal impedance and manometry clarifies esophageal function abnormalities: study in 350 patients. *Am J Gastroenterol* 2004; **99**: 1011-1019

36 **Bredenoord AJ**, Weusten BL, Sifrim D, Timmer R, Smout AJ. Aerophagia, gastric, and supragastric belching: a study using intraluminal electrical impedance monitoring. *Gut* 2004; **53**: 1561-1565

37 **Pandolfino JE**, Shi G, Zhang Q, Ghosh S, Brasseur JG, Kahrilas PJ. Measuring EGJ opening patterns using high resolution intraluminal impedance. *Neurogastroenterol Motil* 2005; **17**: 200-206

38 **Simrén M**, Silny J, Holloway R, Tack J, Janssens J, Sifrim D. Relevance of ineffective oesophageal motility during oesophageal acid clearance. *Gut* 2003; **52**: 784-790

39 **Savoye G**, Savoye-Collet C, Oors J, Smout AJ. Interdigestive transpyloric fluid transport assessed by intraluminal impedance recording. *Am J Physiol Gastrointest Liver Physiol* 2003; **284**: G663-G669

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