

PRINCIPLES OF COMBINED ESOPHAGEAL IMPEDANCE-PH MONITORING IN CHILDREN: INDICATIONS, BENEFITS AND LIMITATIONS

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ABSTRACT

The standard test for suspected gastroesophageal reflux is pH monitoring. However, the majority of gastroesophageal reflux episodes in infants and children are nonacidic (pH > 4) and extraesophageal symptoms apparently can be caused by both acidic (pH < 4) and nonacidic reflux.

In order to overcome these aspects, a new technique has been developed and placed under scrutiny in the past twenty years: multichannel intraluminal impedance. Combined with standard pH recording, it provides more information than simple pH measurement because it allows the study of non-acid reflux and the temporal association between symptoms and nonacid reflux. Data can be analyzed for bolus composition (gas, fluid, solid) and reflux height, duration, and clearance.

Although normal values for the pediatric population are not yet available, combined multichannel intraluminal impedance and pH measurement has the potential to become the new "gold standard" for gastroesophageal reflux testing.

Keywords: children, adolescents, gastroesophageal reflux, esophageal impedance, esophageal pH monitoring, combined esophageal impedance-pH monitoring, esophagus, gastroesophageal reflux, diagnosis, medical

INTRODUCTION

Gastroesophageal reflux (GER) is the involuntary passage of gastric contents into the esophagus and is a normal physiological process occurring several times per day in every human, particularly after meals. Healthy and sick individuals do not differ in the presence or absence of GER, but in the frequency, duration, and intensity of GER and in its association with symptoms or complications. Gastroesophageal reflux disease (GERD) occurs when GER is accompanied by symptoms and complications that impair the quality of life (1).

The only test which addresses directly GER is ambulatory esophageal pH monitoring. Esophageal pH monitoring was developed during the 1960s. Sensitivity and specificity of this test are higher than 80 and 90%, respectively (2).

But esophageal pH monitoring has its limits: it detects acid reflux, but underestimates total reflux. Not least, esophageal pH-metry is unable to determine a cause and effect relationship between refluxes and the observed symptoms (3). Esophageal pH monitoring is also unable to assess the height of reflux and bolus transit (4).

To overcome all these problems, combined pH-impedance measurement devices have been developed since the early 1990s and became available for children of all age groups since 2002 (4,5).

PRINCIPLES OF MULTICHANNEL INTRALUMINAL IMPEDANCE

Multichannel intraluminal impedance (MII) is a technique used to detect the movement of fluids, air

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and solids in a lumen. Detection is based on changes in resistance to the flow of an electrical current between two electrodes surrounded by air, fluids or solids.

In the esophagus, the baseline current is conducted between the rings by ions on the mucosa. Impedance catheters have multiple sets of impedance-measuring rings. Changes in resistance of alternating electrical current passing through these pairs of metal rings on a pH catheter allows the assessment of bolus movement, and the sequence of these changes, the direction (antegrade or retrograde) (5).

When a liquid bolus passes the metal rings, the impedance (resistance) rapidly decreases because of increased ion conductivity through the liquid, returning to baseline once the bolus has passed. A liquid swallow causes impedance to decrease sequentially from the proximal to distal esophagus, whereas liquid gastroesophageal reflux causes impedance to decrease sequentially in a retrograde manner. Air conducts current poorly (ie, it has a high impedance), so air boluses that are swallowed or belched are detected by a dramatic increase in impedance (5).

INDICATIONS OF MII-PH MONITORING

Indications for MII-pH monitoring include:

- Gastrointestinal symptoms (failure to thrive, persistent food refusal, odinophagia, dyspeptic symptoms, vomiting, hematemesis)
- Pulmonary/laryngopharyngeal/ear-nose-throat symptoms (recurrent pneumonia, chronic intermittent cough, apnea, stridor, hoarseness, apparent life-threatening events, globus sensation, dental erosions)
- Neurological indications (dystonic head posturing, children at high risk for GERD due to neurological impairment, developmental delay)
- Patients not responding to empiric antireflux treatment
- Surgical conditions (esophageal atresia, achalasia, postoperative after esophageal surgery)
- Research

MII-pH is particularly useful for the assessment of discontinuous symptoms, such as cough, dysphagia, apnea, dystonic head posturing (Sandifer syndrome). MII-pH can be performed off and/or on treatment and on either continuous or bolus-based enteral feeds, which means that reflux during meals and during postprandial periods should preferably be taken into account (4).

EQUIPMENT

Impedance equipment is more expensive than simple pH metry devices. For pediatric gastroenterologists, useful features are a time indication on the display of the recording device (which allows the parent to accurately log events in real time) and the protection of event marker(s) buttons to avoid erroneous recordings by the child (6). The data recorder is integrated with each manufacturer's catheter. Catheters are compatible only with data recorders from the same company.

Catheters with internal reference electrode are more convenient because no separate external skin electrode is required. Yet this poses a problem as the internal reference electrode is located at the tip of the catheter, which is at least 3 cm distal to the distal pH sensor and may cross the lower esophageal sphincter, thereby potentially increasing the number of GER episodes (7). The standard duration of the recording should be close to 24 hours (at least 18 hours to be conclusive), including a day and a night period both for pH and impedance measurements (8,9).

ADVANTAGES OF MII-PH MONITORING

Besides allowing measurements of acid GER and chemical clearance of the esophagus, combined MII-pH monitoring brings in several important advantages, making it the gold standard in GER assessment:

- It identifies weakly-acid and alkaline reflux.
- It identifies superimposed acid reflux and postprandial GER.
- It detects gas reflux events.
- It assesses the height of reflux episodes.
- It assesses bolus clearance (MII can detect extremely small bolus volumes).
- MII-pH monitoring can distinguish volume clearing from acid clearing (10).
- Low baseline impedance levels detected through MII-pH monitoring are a predictor for the presence of esophagitis (11,12).

The direction and velocity of a bolus can be calculated using the defined distance between electrodes and the time between alterations in the impedance pattern of sequential electrode pairs. The upward extent of the bolus and the physical length of the bolus can also be evaluated. (13).

INTERPRETATION

There are no normal ranges currently available for impedance in children (6). An abnormal number

of reflux episodes is arbitrarily defined as >70 episodes in 24 hours in patients ages 1 year or older and >100 episodes in those younger than 1 year, although a rationale for these cut-off values does not exist yet. A reflux index above 7% is considered as abnormal, a reflux index below 3% as normal, and a reflux index between 3 and 7% as indeterminate (6).

Three parameters are useful in the statistical analysis:

a) the symptom index (SI) represents the number of reflux-related symptoms in the total number of symptom episodes ($\times 100\%$) and is considered to be positive when $> 50\%$. However, studies with a small number of symptoms and/or a high number of GER episodes will yield a false-positive SI.

b) the symptom sensitivity index (SSI, reported as %) is the percentage of symptom-associated GER events divided by the total number of GER events. A value of $>10\%$ is significant here. Here again, studies with a high number of symptoms and/or a small number of GER episodes have a tendency to give a falsely high SSI.

c) the symptom association probability (SAP) represents the likelihood that the patient's symptoms are related to reflux and is calculated analyzing consecutive 2-minute segments, before and after a recorded event. By agreement, the SAP is considered to be positive when it is $> 95\%$ (14)

LIMITATIONS OF IMPEDANCE MONITORING

MII-pH monitoring has currently several limitations:

1. The tracing needs to be interpreted by a trained physician; reading an impedance tracing has a steep learning curve. Tracings with a low baseline are sometimes impossible to interpret, but this occurs mainly in patients with esophagitis where MII-pH monitoring has little role (10). On the other hand, one study found that interobserver agreement in combined MII-pH analysis in experts is moderate, only 42% of GER episodes being detected by the majority of observers (15).

2. Occasionally, pH monitoring records a large number of "pH-only" GER, with debatable meaning (16).

3. Feeding during pH monitoring is an area of controversy: forbidding acid food is recommended, but a restricted diet might alter the patient's normal dietary habits and the results (6).

4. There are rare but potential complications: technical failure, probe misplacement in a bronchus, and mucosal bleeding (4).

5. Recent data show that manual documentation of events in a diary or even using the event button has limitations regarding the precision of the documentation (17). Studies in adults suggest that the delay between the onset of a symptom and the patients' mark on the recording system can be longer than the standard interval considered for automatic analysis (14).

In infants and children, combined pH-MII monitoring increases the likelihood of demonstrating a positive GER-symptom association compared with standard pH monitoring alone. Infants have a predominance of weakly acidic bolus GER caused by pH buffering by more frequent milk feedings (18), and impedance is useful in detecting those events. Inclusion of gas-bolus GER, in addition to liquid and mixed-bolus GER, improves the GER-symptom association (16).

Overall, MII-pH monitoring yields more information than standard pH measurement because it allows the study of non-acid reflux and the temporal association between symptoms and nonacid reflux. Studies in adults have shown that impedance monitoring detects 97-98% of acid reflux detected by the simple pH probe in healthy subjects and patients with GERD, and also $>93\%$ of nonacid and superimposed acid reflux (19-21).

To conclude, studies in adults and children suggest that combined multichannel intraluminal impedance and pH measurement has the potential to become the new "gold standard" for gastroesophageal reflux testing (22).

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