

## Gastric motor and sensory function testing

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### 1. Introduction

Whenever a patient presents with gastrointestinal symptoms, conventional diagnostic means (endoscopical, histological, radiological, biochemical) are used to identify an underlying histological, biochemical, or structural abnormality that could consistently explain the patient's symptoms. When no such cause can be found, the patient's condition is referred to as "functional" as opposed to "organic" disease (1).

Functional bowel disorders may be characterized by symptoms that are attributable to the pharynx, the esophagus, the stomach, the biliary tract, the small intestine, the colon or the anorectum. It is generally assumed that disorders of motor or sensory function underlie these symptoms. Hence, a number of methods have been developed to study the motor and sensory function of the organ to which functional bowel symptoms are attributed.

In a number of patients, symptoms are related to feeding and include epigastric pain, bloating, early satiety, fullness, anorexia, belching, nausea and vomiting. As these symptoms suggest a disturbance of gastric function, a number of methods have been developed to study the motor (and sensory) function of the stomach.

### 2. Classification of gastric motor disorders

Prior to making a diagnosis of a gastric motor disorder, organic disease, especially mechanical obstruction, has to be ruled out. Gastric motor disorders can either be primary, i.e. that no apparent underlying cause is present, or secondary, i.e. that they are related to another medical condition of the patient. The primary and secondary gastric motor disorders are listed in Table I.

Of the primary gastric motor disorders, functional dyspepsia has been studied most intensively. It is unclear whether the idiopathic gastroparesis syndrome constitutes a separate entity, or falls within the spectrum of functional dyspepsia. Gastro-esophageal reflux disease and chronic idiopathic pseudo-obstruction syndromes, in which the main organ that is dysfunctional is not the stomach, will not be further addressed.

Of the secondary gastric motor disorders, metabolic and more specifically diabetic gastroparesis is the most common condition. Other important causes constitute postsurgical states (e.g. after anti-reflux surgery), visceral myopathies (e.g. systemic sclerosis), drug-induced (e.g. antidepressants) and central nervous system disorders (e.g. cerebral tumors).

When studying secondary gastric motor disorders, the main goal is to document whether or not the disorder is present. For instance, in a patient with diabetes, one may want to document whether or not diabetic gastroparesis is present. In contrast, when studying patients with presumed primary gastric motor disorders, the goal is mainly to establish or confirm a diagnosis (e.g. idiopathic gastroparesis) and, if possible, also to direct therapeutic efforts.

### 3. Diagnostic tools to study gastric motor function

The measurement of gastric emptying rate is the test which is used most frequently to assess gastric function. Several techniques are available to study the gastric emptying rate of solid or liquid meals. In most in-

Table I. — Primary and secondary gastric motor disorders

<i>Primary gastric motor disorders</i>
Functional dyspepsia
Idiopathic gastroparesis
Idiopathic cyclical nausea and vomiting syndrome
Aerophagia
Rumination syndrome
Gastro-esophageal reflux disease
Idiopathic chronic pseudo-obstruction
<i>Secondary gastric motor disorders</i>
Metabolic disorders
Postsurgical
Central nervous system disorders
Extrinsic neuropathy
Drug-induced gastric motor disorders
Intestinal neuropathy
Intestinal myopathy

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stances, the measurement of solid gastric emptying is clinically most relevant. When documenting suspected dumping syndrome, it may be valuable to assess liquid emptying as well.

The use of a radiolabeled meal, and scintigraphic measurement of the proportion of tracer present in a region of interest depicting the stomach is the most widely used test to measure gastric emptying (2,3). Depending on the label used, solid and also liquid emptying can be assessed. More recently, a gastric emptying breath test was developed, using  $^{13}\text{C}$  octanoic acid as a marker for the solid phase and  $^{14}\text{C}$  glycine for the liquid phase (4,5). In the literature, a number of other tests to assess gastric emptying are described, but these are often unvalidated, experimental, or limited to liquid emptying only (6-13). In clinical practice, scintigraphy or the breath test are generally used.

A more direct method to study gastric motor function is manometry, most frequently carried out using a catheter that has ports both in the stomach and in the proximal small intestine (14-17). Gastrointestinal manometry is limited to stationary studies, as unpredictable catheter movement is occurring when trying to carry out ambulatory antroduodenal manometry. In stationary studies, manometry allows to document the presence of normal interdigestive motility, to show conversion to a postprandial motor pattern, and to quantify postprandial antral motility. However, application of this technique is limited to tertiary referral centers and even there it has mainly an academic and experimental interest. When testing the presence of a normal MMC pattern, prolonged recording time is necessary, and the most frequently used time interval of 3 to 4 hours is inappropriate to document absence of normal interdigestive motility (16,17). Moreover, when one wants to administer a meal and register return to interdigestive motility, marked by the presence of phase 3 of the migrating motor complex, extremely prolonged recordings are required. After a meal of 1700 kJ, up to 10 hours may be required (17). This implies that a stationary recording wanting to adequately assess both interdigestive and postprandial motility should last at least 10 hours. This is unpractical, and would require a high diagnostic impact of such a test. Unfortunately, this is not true for gastroduodenal manometry. It has been demonstrated that delayed gastric emptying of solid food is associated with antral hypomotility, resulting in gastric stasis (18). In addition, in patients with pseudo-obstruction syndrome and in radiation enteropathy, mainly aberrant configuration and migration of intestinal phase 3 were found to be indicators of a major motor disorder (19,20). Hence, we feel that gastroduodenal manometry is presently mainly a research tool.

The latest addition to techniques used to study gastric function is the gastric barostat. It is used to study changes in tone and to study the sensitivity to distention of the proximal stomach. To perform barostat studies, a double lumen polyvinyl tube with an

adherent plastic bag of up to 1200 mL capacity is introduced into the proximal stomach. The polyvinyl tube is then connected to a barostat device which monitors pressure with the bag, and keeps it constant by adjusting the intra-bag volume (fig. 1). The barostat can maintain a constant pressure, in which case volume changes reflect changes in proximal gastric tone, for instance after the administration of a meal or a drug (21). Alternatively, the barostat can deliver pressure steps at a certain rate, while simultaneously monitoring intrabag volume and asking the subject to score the perception of upper abdominal sensations induced by each distending stimulus. This allows to determine the thresholds for perception and discomfort during gastric distention (22).

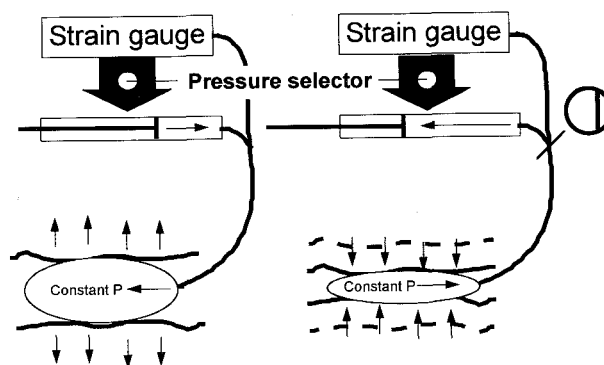


Fig. 1. — Principle of barostat studies of the proximal stomach. A set intra-balloon pressure is maintained constant by adapting the intra-balloon volume. In case of a relaxation of the organ (left), the barostat pumps more air into the bag to maintain a constant pressure. In case of a relaxation of the organ (right), the barostat pumps air out of the bag to maintain a constant pressure.

In the next paragraphs, we will mainly address scintigraphic measurement of gastric emptying and barostat assessment of gastric sensitivity to distention and of gastric accommodation to a meal.

#### 4. Targets for studies of gastric motor function

In order to achieve a maximal clinical impact, an ideal clinically applied test should have a number of characteristics. First of all, it should have diagnostic specificity, i.e. that a certain finding of the test would lead to a single and unique diagnosis. Second, it should be able to explain the symptoms that made the patient come to medical attention. Third and fourth, it should determine the choice of therapy and preferably also be able to predict a response to therapy. Finally, a diagnostic test should ideally also provide some predictive information regarding the prognosis of the underlying condition. Unfortunately, when judging gastric function test by these standards, we find out we have a long way to go.

#### 4.1. Diagnostic specificity

The currently used test to study gastric function do not yield a high diagnostic sensitivity. Delayed gastric emptying and antral hypomotility, for instance, are present in the majority of patients with anorexia nervosa (23,24). Hence, a finding of a delayed gastric emptying or antral hypomotility by itself has no diagnostic specificity, even in the absence of underlying organic or metabolic pathology. Similarly, one can find rapid gastric emptying, especially of liquids, in patients with dumping syndrome (25). Nevertheless, a diagnosis of dumping syndrome cannot be made on the basis of rapid emptying, but it requires specific tests or observations. Using the gastric barostat, one can demonstrate impaired accommodation of the proximal stomach to a meal in a subset of patients with functional dyspepsia (26). Nevertheless, a similar disorder has been reported in diabetic patients (27). Hence, barostat findings too seem to carry little diagnostic specificity.

#### 4.2. Explanation of symptoms

Concerning gastric motor disorders, most studies have failed to establish a clear relationship between putative pathophysiological disturbances and symptom production. Several studies failed to find a correlation between delayed gastric emptying and symptoms in patients with functional dyspepsia (28-32). Recently, Stanghellini *et al.* were able to demonstrate that dyspeptic patients with delayed gastric emptying were more likely to suffer from postprandial fullness and vomiting (33). Usting scintigraphy, Troncon *et al.* demonstrated an abnormal intragastric distribution of food during gastric emptying in patients with severe postprandial bloating, but no attempt was made to correlate the abnormality to symptom severity (34). Gilja *et al.*, using ultrasound, could not demonstrate a correlation between impaired gastric accommodation to a meal and global symptom severity, but individual dyspeptic symptoms were not assessed (35).

We studied 75 consecutive patients in which a diagnosis of functional dyspepsia was made after clinical assessment, laboratory tests, upper gastrointestinal endoscopy and abdominal ultrasound (36). Each patient presented to the outpatient clinic of our tertiary referral center because of meal-related epigastric symptoms, and underwent careful history taking and clinical examination, upper gastrointestinal endoscopy, routine biochemistry and upper abdominal ultrasound. Inclusion criteria were the presence of dyspeptic symptoms lasting for at least 3 months, in the absence of organic, systemic or metabolic disease, as well as obvious psychiatric illness. Dyspeptic symptoms had to be present at least three days per week, with two or more symptoms scored as relevant or severe on the symptom questionnaire (see below). Exclusion criteria were the presence of esophagitis, gastric atrophy or erosive

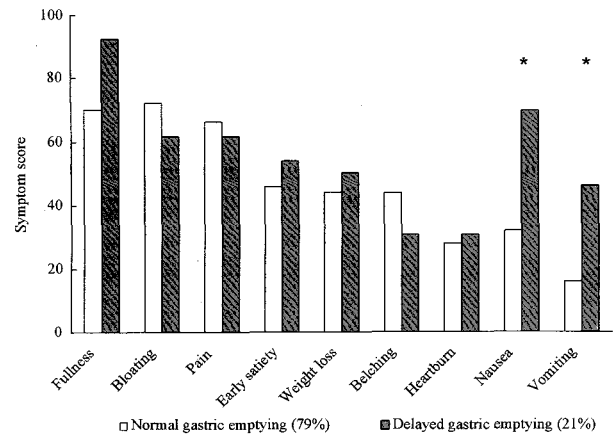


Fig. 2. — Symptom patterns in patients with functional dyspepsia. The figure depicts the number of patients grading individual symptoms as relevant or severe (score 2) in the subgroups with normal or delayed gastric emptying. Nausea and vomiting were significantly more prevalent in patients with delayed gastric emptying.

gastroduodenal lesions on endoscopy, heartburn as a predominant symptom, a history of peptic ulcer, major abdominal surgery, and the use of nonsteroidal anti-inflammatory drugs, steroids or drugs affecting gastric acid secretion. In each patient, the severity (0-3, 0 = absent, 1 = mild, 2 = relevant, 3 = severe) of six dyspeptic symptoms (epigastric pain, bloating, early satiety, fullness, belching, epigastric burning, nausea and vomiting) was scored as absent, mild, relevant or severe, and the presence or absence of weight loss was noted. Each patient underwent a gastric emptying study using the octanoic acid breath test. In 60 patients, a gastric barostat procedure was performed to assess the sensitivity of the stomach to gastric distention and in 40 patients to study gastric accommodation to a mixed liquid meal.

Delayed solid gastric emptying was present in 21% of the patients. They had significantly more relevant or severe nausea and vomiting ( $p < 0.05$ ) (fig. 2). Using isobaric distentions during gastric barostat studies, hypersensitivity to gastric distention was found in 55% of the patients. This was associated with significantly more relevant or severe postprandial fullness ( $p < 0.005$ ). We used a gastric barostat to study postprandial fundus relaxation in 35 healthy subjects and in 40 patients with functional dyspepsia. Compared to the normal range in healthy controls, 40% of the dyspeptic patients had an insufficient relaxatory response after a meal (less than mean - 2 standard deviations). This was accompanied by lower thresholds for perception and for discomfort during postprandial gastric distentions. Patients with impaired fundus relaxation had significantly higher scores for early satiety ( $p < 0.001$ ), and a significantly higher prevalence of weight loss ( $p < 0.01$ ) (fig. 3).

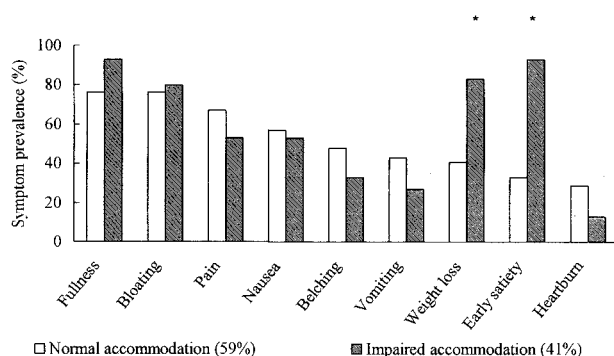


Fig. 3. — Symptom patterns in patients with functional dyspepsia. The figure depicts the number of patients grading individual symptoms as relevant or severe (score 2) in the subgroups with normal or impaired gastric accommodation to a meal. Early satiety and weight loss exceeding 5% of the initial body weight were significantly more prevalent in patients with impaired accommodation to a meal.

Hence, functional studies of the stomach are able to explain a number of symptoms in patients with gastric motor or sensory abnormalities.

#### 4.3. Determination of the choice of therapy

At present, our abilities to treat gastric motor and sensory disorders are extremely limited. In case of dyspeptic symptoms, in the presence or absence of delayed gastric emptying, prokinetic drugs will generally be used. In the rare case of dumping syndrome, dietary measures and occasionally octreotide will be used. In view of the limited therapeutic possibilities, gastric function tests will generally not determine a choice of therapy. However, if drugs become available that will improve gastric hypersensitivity, or that will restore impaired gastric accommodation to a meal, the role of gastric function testing, especially using the barostat, may expand.

#### 4.4. Prediction of response to therapy

Here, the same limitation applies: by lack of therapeutic alternatives, prediction of the response to therapy will be of limited value. Two studies have suggested that the response to prokinetic therapy in

functional dyspepsia might be better in patients with delayed gastric emptying than in those with normal gastric emptying (37,38). It is unknown whether patients with for instance hypersensitivity to gastric distention or impaired gastric accommodation to a meal would react differently to prokinetic drug therapy than those in whom these functions are still normal. In one study, dyspeptic patients were treated with a tricyclic antidepressant, assuming that this would improve hypersensitivity to gastric distention (39). However, no correlation was found between symptomatic improvement and the evolution of gastric hypersensitivity.

#### 4.5. Prognostic information

At present, it is unknown whether the results of gastric function testing will have an impact on the prognosis of patients with presumed gastric motor disorders.

### 5. Conclusion

The clinical impact of gastric function tests is at present rather limited. The data are summarized in table II. The currently available tests allow us to study gastric emptying, gastric motor activity, gastric sensitivity to distention and gastric accommodation to a meal. Each of the available tests lack diagnostic specificity; they can yield similar abnormalities under a number of different circumstances. The best application of these tests seems to be in the explanation of symptoms. It has been shown — although some of these data are still preliminary — that both gastric emptying test and gastric barostat studies are able to explain some symptoms. No data are available on the prognostic value of gastric motor and sensory function tests.

In daily practice, we feel that patients with a presumed gastric motor disorder — except in the case of suspected dumping syndrome — can receive standard prokinetic therapy, as this is the only valid therapeutic option (fig. 4). In those who do not respond appropriately to this type of therapy, our approach is to conduct gastric function tests. Depending on the result that these tests yield, we would start therapy in an experimental study protocol using newer prokinetics (e.g. motilides) or fundus-relaxing drugs. The main use of gastric function testing, therefore, is in an experimental setting.

Table II. — Summary of the clinical impact of gastric function tests

	Gastric emptying	Gastric manometry	Gastric barostat
Diagnostic specificity	No	No	No
Explanation of symptoms	Yes	Unknown	Yes
Determination of therapy	Not at present	Not at present	Not at present
Prediction of response to therapy	Yes	Unknown	Unknown
Prognostic value	Unknown	Unknown	Unknown
Experimental use	Yes	Yes	Yes

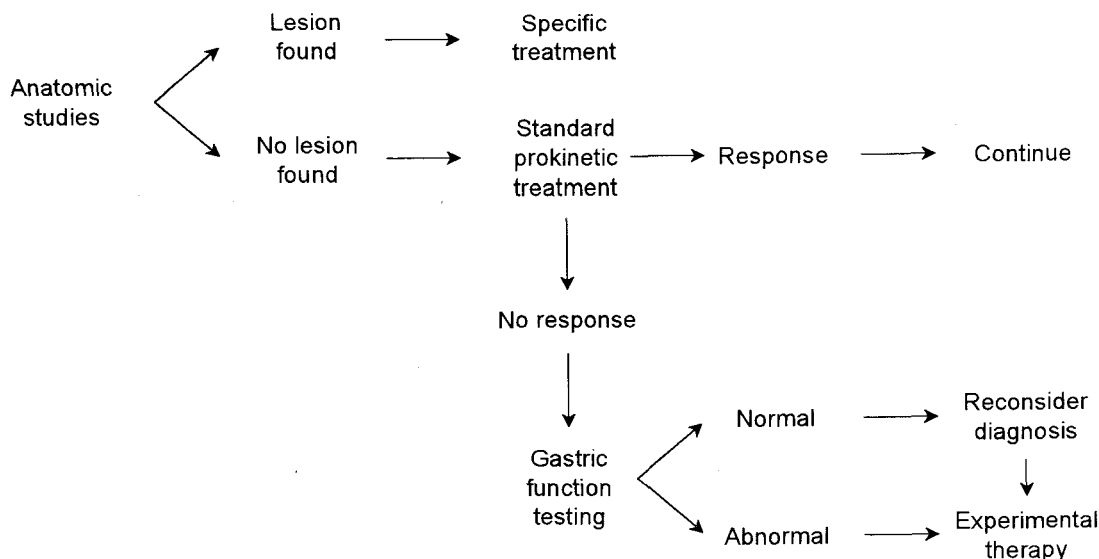


Fig. 4. — Clinical approach to a patient with a suspected primary gastric motor disorder.

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