World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/1007-9327office
wjg@wjgnet.com
doi:10.3748/wjg.v18.i14.1555

World J Gastroenterol 2012 April 14; 18(14): 1555-1564
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

EDITORIAL

Consensus statement AIGO/SICCR: Diagnosis and treatment of chronic constipation and obstructed defecation (part Ⅰ: Diagnosis)

Antonio Bove, Filippo Pucciani, Massimo Bellini, Edda Battaglia, Renato Bocchini, Donato Francesco Altomare, Giuseppe Dodi, Guido Sciaudone, Ezio Falletto, Vittorio Piloni, Dario Gambaccini, Vincenzo Bove

Antonio Bove, Vincenzo Bove, Gastroenterology and Endoscopy Unit, Department of Gastroenterology, AORN "A. Cardarelli", 80131 Naples, Italy
Filippo Pucciani, Department of Medical and Surgical Critical Care, University of Florence, 50141 Florence, Italy
Massimo Bellini, Dario Gambaccini, Gastrointestinal Unit, Department of Gastroenterology, University of Pisa, 56100 Pisa, Italy
Edda Battaglia, Gastroenterology and Endoscopy Unit, Cardinal Massaja Hospital, 14100 Asti, Italy
Renato Bocchini, Gastroenterology Unit, M. Bufalini Hospital, 47023 Cesena, Italy
Donato Francesco Altomare, Department of Emergency and Organ Transplantation, University of Bari, 70124 Bari, Italy
Giuseppe Dodi, Department of Oncological and Surgical Sciences, University of Padua, 35126 Padua, Italy
Guido Sciaudone, Division of General and Geriatric Surgery, Second University of Naples, 80131 Naples, Italy
Ezio Falletto, Sixth Division of University Surgery, Department of General Surgery, San Giovanni Battista Hospital, 10126 Turin, Italy
Vittorio Piloni, Diagnostic Imaging Centre "N. Aliotta", Villa Silvia - Senigallia, I-60100 Ancona, Italy
Author contributions: Bove A, Pucciani F and Bellini M contributed to the study concept and design; Battaglia E, Bocchini R, Altomare DF, Dodi G, Sciaudone G, Falletto E and Piloni V collected data and wrote the manuscript; the manuscript was revised by Gambaccini D and Bove V; all authors read and approved the paper.
Supported by Associazione Italiana Gastroenterologi and Endoscopisti Digestivi Ospedalieri via N Colajanni, 4 - 00191 Roma, Italy; and Società Italiana di Chirurgia Colo-Rettale via Medici, 23 - 10143 Torino, Italy
Correspondence to: Antonio Bove, MD, Gastroenterology and Endoscopy Unit, Department of Gastroenterology, AORN "A. Cardarelli", Via Cardarelli, 9, 80131 Naples, Italy. 3392982380@fastwebnet.it
Telephone: +39-81-7474034 Fax: +39-81-7474034
Received: July 31, 2011 Revised: October 21, 2011
Accepted: March 10, 2012
Published online: April 14, 2012

Abstract

Chronic constipation is a common and extremely troublesome disorder that significantly reduces the quality of life, and this fact is consistent with the high rate at which health care is sought for this condition. The aim of this project was to develop a consensus for the diagnosis and treatment of chronic constipation and obstructed defecation. The commission presents its results in a "Question-Answer" format, including a set of graded recommendations based on a systematic review of the literature and evidence-based medicine. This section represents the consensus for the diagnosis. The history includes information relating to the onset and duration of symptoms and may reveal secondary causes of constipation. The presence of alarm symptoms and risk factors requires investigation. The physical examination should assess the presence of lesions in the anal and perianal region. The evidence does not support the routine use of blood testing and colonoscopy or barium enema for constipation. Various scoring systems are available to quantify the severity of constipation; the Constipation Severity Instrument for constipation and the obstructed defecation syndrome score for obstructed defecation are the most reliable. The Constipation-Related Quality of Life is an excellent tool for evaluating the patient's quality of life. No single test provides a pathophysiological basis for constipation. Colonic transit and anorectal manometry define the pathophysiologic subtypes. Balloon expulsion is a simple screening test for defecatory disorders, but it does not define the mechanisms. Defecography detects structural abnormalities and assesses functional parameters. Magnetic resonance imaging and/or pelvic floor sonography can further complement defecography by providing information on the movement of the pelvic floor and the organs that it supports. All these investigations are indicated to differentiate

between slow transit constipation and obstructed defecation because the treatments differ between these conditions.

Key words: Slow transit constipation; Dyssynergic defecation; Obstructed defecation; Constipation scoring system; Quality of life; Anorectal manometry; Colon motility; Balloon expulsion test; Defecography

Peer reviewers: Venkatesh Shanmugam, MBBS, MS, Dip. NB, FRCS, MD, Specialist Registrar, Royal Derby Hospital, Uttoxeter Road, Derby, DE22 3NE, United Kingdom; Wallace F Berman, MD, Professor, Division of Pediatric GI/Nutrition, Department of Pediatrics, Duke University Medical Center, Duke University School of Medicine, Durham, Box 3009, NC 27710, United States

Bove A, Pucciani F, Bellini M, Battaglia E, Bocchini R, Altomare DF, Dodi G, Sciaudone G, Falletto E, Piloni V, Gambaccini D, Bove V. Consensus statement AIGO/SICCR: Diagnosis and treatment of chronic constipation and obstructed defecation (part I : Diagnosis). *World J Gastroenterol* 2012; 18(14): 1555-1564 Available from: URL: http://www.wjgnet.com/1007-9327/full/v18/i14/1555.htm DOI: http://dx.doi.org/10.3748/wjg.v18.i14.1555

INTRODUCTION

The mission of the Italian Association of Hospital Gastroenterologists (AIGO) is to advance the knowledge of digestive pathologies, to promote progress in the prevention, diagnosis, care and rehabilitation of gastrointestinal diseases, and to promote research.

The aim of the Italian Society of Colo-Rectal Surgery (SICCR) is to ensure the highest therapeutic standards through the evaluation and introduction into medical practice of the latest advances in the areas of prevention, diagnosis and care of pathologies involving the colon, rectum and anus.

The Joint Committee AIGO/SICCR is made up of members of these two scientific societies, elected on the basis of their experience in treating functional and organic problems of the colon and rectum.

The objective of the committee was to develop a consensus statement on the most important diagnostic and therapeutic aspects of functional constipation and obstructed defecation, including a set of graded recommendations based on a review of the literature and on evidence-based medicine.

LITERATURE SEARCH

A search of the literature was carried out using the online databases of PUBMED, MEDLINE and COCHRANE to identify articles published in English before April 2011 and reporting trials conducted on adult subjects with chronic constipation. The key words used were: Rome criteria, constipation, slow transit constipation, pelvic floor dyssynergia, dyssynergic defecation, dyschezia, colonic inertia, bowel questionnaire, constipation scoring system, quality of life, anorectal manometry, rectal compliance, colonic transit, colon motility, gastrointestinal motility, colonic manometry, balloon expulsion test, pelvic floor imaging, proctography, cystoproctography, dynamic magnetic resonance, anal ultrasound, endosonography, constipation medical therapy, alimentary fibres, laxatives, prokinetics, probiotics, biofeedback, pelvic floor rehabilitation, sacral nerve stimulation, obstructed defecation, outlet obstruction, rectocele, rectal intussusception, rectal prolapse, enterocele, Duhamel operation, Block operation, Sarles operation, stapled transanal resection, Delorme operation, Ripstein operation, colorectal surgery, colectomy, ileorectal anastomosis, segmental colonic resection, laparoscopic colectomy, antiperistaltic cecoproctostomy, cecorectal anastomosis, antegrade colonic enema, Malone's procedure, Malone antegrade continence enema, colostomy, ileostomy, colonic irrigation, pelvic organ prolapse, posterior vaginal prolapse, posterior colporrhaphy, transanal repair, transvaginal repair and mesh.

Table 1 Levels of evidence[1]

Levels of evidence	
I	Randomised clinical trials with $P < 0.05$, adequate sample size, and appropriate methodology
II	Randomised clinical trials with $P < 0.05$, inadequate sample size, and/or inappropriate methodology
III	Non-randomised trials with simultaneous controls
IV	Non-randomised trials with historical controls
V	Case series

LEVELS OF EVIDENCE AND GRADING OF RECOMMENDATIONS

The recommendations of the committee were defined and graded based on the current levels of evidence and in accordance with the criteria adopted by the American College of Gastroenterology's Chronic Constipation Task Force[1].

Five evidence levels were defined (Table 1). The recommendations were graded A, B and C (Table 2).

The committee wishes to underline that insufficient evidence does not automatically imply "evidence against" a statement. Many decisions in daily practice are based on clinical experience. Sometimes, it is difficult to find scientific papers supporting a widespread clinical practice, but this difficulty does not mean that we need to refute or abandon therapies that clinicians have been using for years with their patients. Evidence-based medicine is a useful tool to guide clinical practice, but if applied mechanically and without the application of common sense and personal experience, it can lead to erroneous conclusions[2].

In the development of this consensus statement, the committee identified five key areas (Table 3) and divided

Table 2 Grading of the recommendations[1]

Grading of the recommendations	
A	Recommendation supported by two or more level I trials, without conflicting evidence from other level I trials
B	Recommendation based on evidence from a single level I trial OR, evidence from two or more level I trials with conflicting, evidence from another level I trial OR, evidence from two or more level Ⅱ trials
C	Recommendations based on levels of evidence Ⅲ-V

OR: Odds ratio.

Table 3 Areas defined by the committee for the consensus statement

Area	
1	Clinical evaluation and scoring systems
2	Diagnostic techniques
3	Medical and rehabilitative treatment
4	Surgery for slow transit constipation
5	Surgery for obstructed defecation with or without associated pelvic diseases

them into subsections. Each subsection was researched, and recommendations were prepared by one or more members of the committee in accordance with specific themes defined by the committee.

The process of drafting the consensus statement involved constant communication and evaluation conducted online and during four face-to-face working meetings held at 3-mo intervals. During these meetings, the levels of evidence and the grading of the recommendations were discussed to reach a consensus in all the areas covered in the consensus statement.

The commission presents its results here in a "Question-Answer" format, which will allow clinicians to find concise responses to their specific questions quickly and easily and to peruse the full text at their leisure.

DEFINITION OF CONSTIPATION

Constipation can be either primary or secondary. The commission adopted the definition of primary functional constipation outlined in the Rome Ⅲ criteria[3]. This set of criteria was developed by an international group of experts through a process of consensus, and it has been reviewed and revised more than once since it was first published[3-5].

Stool form was defined using the Bristol stool form score[6]; constipation may involve slow intestinal transit and/or abnormal defecation; the definition of abnormal defecation from the Rome Ⅲ criteria was adopted[7].

CLINICAL EVALUATION AND SCORING SYSTEMS

Clinical evaluation

Is a patient history useful in the evaluation of chronic constipation? A thorough medical history should always be taken in patients with chronic constipation. This process constitutes the first approach to the patient and is designed to detect events that may be directly or indirectly linked to the patient's symptoms[8-11].

The patient history can identify conditions responsible for secondary constipation[11,12], such as the following: (1) alarm symptoms, such as weight loss, bloody stools, anaemia, or a family history of colon cancer; (2) conditions and/or diseases potentially associated with constipation, such as inappropriate diet[13], low physical activity[10], the use of constipating drugs, and metabolic, psychiatric or neurological diseases; and (3) the negative outcome of perineal-pelvic-abdominal or obstetric-gynaecological surgery[14,15].

Can the medical history distinguish among the different subtypes of chronic constipation? No, there are as yet no specific criteria that can distinguish among the subtypes of chronic constipation based on anamnesis[7,16-18]. Level I evidence, Grade A recommendation.

Are there specific symptoms that are present only in patients with functional constipation? No, there are no specific symptoms that distinguish patients with functional constipation from normal subjects[3]. Level I evidence, Grade A recommendation.

The occurrence of two or more symptoms during at least 25% of bowel movements distinguishes patients with chronic constipation from normal subjects[3,19].

Should a physical examination be performed in patients with chronic constipation? A physical examination is essential in the initial workup of a patient with chronic constipation[11]. The examination should include inspection of the anorectal region and exploration of the rectum. This process can detect external signs of anal disease, pelvic organ prolapse, or descending perineum syndrome. A digital rectal examination should detect any signs of organic disease or obstructed defecation. The examination is particularly important if functional alterations in defecation are suspected.

Is blood testing useful in the diagnostic algorithm of functional constipation? Blood testing does not provide useful input. Functional constipation is defined as a primitive condition and is not accompanied by any organic or biochemical alterations, being associated instead with a "functional" pathology of visceral motility. For this reason, there are no laboratory tests for the diagnosis of functional constipation[3,9]. Level I evidence, Grade A recommendation.

Blood tests can, however, be performed to exclude conditions of secondary chronic constipation[12].

Should morphological investigations (colonoscopy, barium enema, or computerised tomographic colonography) be performed in all patients with chronic constipation? Prospective studies on this point are lacking in the literature[20,21]. There is no clear evidence to support the usefulness of colonoscopy in patients with chronic constipation. Level Ⅳ evidence, Grade C recommendation.

However, morphologic investigations should always be performed in patients with alarm symptoms, in patients > 50 years of age, and in patients with a family history of colon cancer.

SCORING SYSTEMS IN CHRONIC CONSTIPATION

Scoring systems to quantify disease severity

Various scoring systems have been developed to quantify the severity of constipation. These systems are particularly important in a subjective, functional disease, such as constipation, to evaluate the results of therapy.

An early scoring system, the chronic idiopathic constipation index (CICI), was published in *Techniques of Coloproctology* in 1996[22]. It is based on seven variables (scored from 0 to 3, with a maximum score of 21) and was designed to detect chronic idiopathic slow transit constipation. The CICI was the first evaluation system that took into consideration signs of autonomic neuropathy. However, it has never been validated in a prospective study.

In 1999, the Patient Assessment of Constipation Symptoms[23] was published. This 12-item, patient-administered questionnaire has been validated and found to be effective, but it is rarely used in clinical studies.

The most widely adopted instrument is the Cleveland Clinic Constipation Score[24]. It is easy to understand and administer and therefore has won broad acceptance, although it has not been formally validated. It consists of 8 items scored from 0 to 4 for a maximum score of 30. It should be noted that one of the items, "duration of symptoms", cannot be modified by therapy.

In 2002, a new, prospectively validated score, the symptom scoring system for constipation[25], consisting of 11 items scored from 0 to 3 or 4 for a maximum possible score of 39, was published, but it is rarely used.

More recently the Constipation Severity Instrument (CSI)[26] was developed. It is a well-designed scoring system consisting of 78 items that can identify and quantify different types of constipation (IBS, slow transit and obstructed defecation).

In 2008, the first instrument specifically designed for obstructed defecation syndrome, the obstructed defecation syndrome (ODS) score, was published in *Colorectal Disease*[27]. It consists of 7 items scored from 0 to 4 with a maximum score of 27, and it has been prospectively validated.

Measuring quality of life in constipation

Three Quality of Life (QoL) questionnaires for constipation have been published. The gastrointestinal QoL questionnaire[28] was designed to address all gastrointestinal symptoms and therefore is not specific for constipation. It includes 36 items with 5 possible answers, and it has a maximum possible score of 180.

In 2005, the first disease-specific questionnaire on constipation appeared, the Patient Assessment of Constipation Quality of Life[29]. It consists of 28 items scored from 0 to 4 with a maximum score of 112.

Recently, a new, statistically validated QoL questionnaire, the Constipation-Related Quality of Life (CRQOL)[30], was published. It includes 4 domains: social impact (11 items), distress (11 items), usual diet (11 items), and defecation features (4 items).

Conclusions

Several scoring systems for constipation can be found in the medical literature. The consensus of the committee is that the most reliable instruments for scoring disease severity are the CSI for constipation in general and the ODS score for obstructed defecation. The CRQOL is an excellent tool for evaluating the effects of constipation on the patient's quality of life. The use of these instruments is recommended for clinical trials.

DIAGNOSIS OF FUNCTIONAL CONSTIPATION

Imaging in chronic constipation and obstructed defecation syndrome

Currently available imaging techniques for chronic constipation and ODS include the following: (1) transit time (TT) studies[31,32]; (2) X-ray videoproctography[33] and colpo-cysto-entero-defecography[34,35]; (3) magnetic resonance (MR)-defecography[36]; and (4) ultrasonography (US) of the pelvic floor[37-40].

Can a TT study differentiate slow transit constipation from obstructed defecation? Depending on the site of accumulation of the radiopaque markers along the large bowel, an initial TT study can differentiate between patients with total or segmental colonic slow transit constipation and patients with outlet obstruction. Unfortunately, lack of standardisation in the procedure makes it difficult to compare results among centres. Level V evidence, Grade C recommendation. In the case of distal obstruction, X-ray defecography is recommended as a second-line examination. The fact that this examination has been universally adopted makes it the benchmark against which to test newer modalities.

When should defecography be performed as opposed to colpo-cysto-entero-defecography? Defecography is indicated to rule out a variety of conditions that could play a role in the aetiology of the presenting symptom(s), such as paradoxical contraction of the puborectalis muscle[41,42], a rectocele, recto-anal intussusception and complete external rectal prolapse. Colpo-cysto-entero-defecography should be performed when multiple compartment defects are suspected, including cystocele, enterocele, or descending perineum syndrome[43].

Because their clinical significance remains a matter of debate, there is general agreement[44-46] that the results of contrast radiography should not be relied on exclusively when making decisions regarding the treatment of a patient (including surgery).

When should MR defecography be considered as an alternative to X-ray examination? Due to the panoramic

view that they provide and the absence of ionising radiation, MR imaging of the pelvic floor and MR defecography are now frequently recommended as a valid alternative to contrast radiography, especially in young patients, female patients of reproductive age, pregnant patients, and those patients at risk for adverse reactions to the contrast medium.

Are the findings commonly observed on defecography captured equally well by MR defecography? Despite the less natural (horizontal) position of the patient during the exam, MR imaging can provide similar, and sometimes better, results than conventional X-rays, with the added advantage (especially in the case of defects affecting multiple compartments) of the superior reproducibility of the results[47,48]. Consequently, while MR defecography is widely recommended as a tool to increase diagnostic confidence in cases of evacuation dysfunctions, MR neurography of the pelvic floor can be extremely useful in detecting pudendal nerve entrapment neuropathy in patients with chronic pelvic pain[49]. Level V evidence, Grade C recommendation.

Can defecographic findings be assessed and measured by perineal, endovaginal and endoanal sonography? There has been a reappraisal of the use of perineal, introital, endoanal and endovaginal US (conventional 2-D and 3-D images recorded using a variety of probes: convex, end-fire, linear and axial 360° rotating models) in the evaluation of the pelvic floor anatomy in patients with evacuation dysfunctions[50-55]. With the exception of rectal evacuation[56], the presence and severity of the most common ODS abnormalities visible on defecography can be equally well documented by any one of these sonography techniques. Level V evidence, Grade C recommendation.

What is the role of endovaginal sonography in chronic constipation? Currently, 2-D and 3-D endovaginal sonography are recommended as alternatives to defecography and MR imaging, respectively, when assessing the overall anatomic configuration and movement of the urogenital hiatus in patients with multiple defects affecting the muscular and fascial components of various compartments (anterior, middle and posterior), which are possibly indicative of descending perineum syndrome or pelvic organ prolapse[53,54]. Level V evidence, Grade C recommendation.

What is the role of endoanal sonography in chronic constipation? Given the inherently static nature of this examination and the presence of a foreign object in the anal canal (i.e., the endocavitary probe), endoanal sonography is of limited value in the diagnosis of chronic constipation. Recently, however, the advent of 3-D reconstruction has significantly increased the diagnostic confidence associated with this technique[55], which can provide detailed imaging of abnormalities, such as the extent of anal sphincter defects, the anatomy of fistulous tracts in complex perianal sepsis, and submucosal invasion in early anorectal cancers.

In summary, general agreement exists among authors that the first-line examination remains TT, followed by X-ray defecography. When the appropriate instruments and trained personnel are available, MRI and/or pelvic floor sonography can further complement defecography by providing information on the movement of the pelvic floor and the organs that it supports.

Anorectal manometry

Anorectal manometry measures anal canal pressures. Perfusion catheters are generally employed, rather than solid-state microtransducers, which are more reliable but too expensive for routine use[57]. Vector volume manometry has been developed to provide a 3-D view of the anal sphincter, but its clinical utility is still under evaluation[58]. Recently, the high-resolution manometry has been shown to provide grater details than water-perfused manometry, but it is still in the experimental stage[59].

The reproducibility of anal manometry is high[60], but its reliability depends on the operator's experience, and its utility is limited by the absence of standardised protocols[61,62] and of data from large numbers of normal subjects[57,63]. Moreover, most of the parameters measured by anorectal manometry (anal canal pressure, sensory thresholds) are influenced by sex and age[64].

Should anorectal manometry always be performed in patients with chronic constipation and/or obstructed defecation? The main indication for anorectal manometry is the presence of obstructed defecation[65,66]. It should also be performed in patients who do not improve with first-line treatments for chronic constipation (a defecation disorder is reported in 51% of such patients)[12,67].

Anorectal manometry, together with other tests, can provide essential information on the rectoanal function defects involved in the physiopathology of obstructed defecation, including increased pressure in the anal canal, rectoanal inhibitory reflex defects, lower rectal sensitivity, and increased rectal compliance[7]. Level Ⅱ evidence, Grade B recommendation.

Is anorectal manometry sufficient for the diagnosis of obstructed defecation? There is no gold standard for the diagnosis of obstructed defecation, and manometry alone does not provide sufficient grounds for the diagnosis. A comprehensive evaluation of anorectal function is necessary and should include tests to evaluate various aspects of defecation, including the balloon expulsion test, imaging techniques, and perhaps electromyography, in addition to manometry[7]. Defecography can evaluate the morphological and dynamic factors of defecation; anorectal manometry measures anorectal sensitivity and motility; and electromyography can provide information on electrical activity in the external anal sphincter muscle during straining. The balloon expulsion test can confirm the diagnosis of obstructed defecation[68,69]. Level Ⅱ evidence, Grade B recommendation.

Anorectal manometry consists of several tests; which of them are most useful in the diagnosis of obstructed defecation? At a minimum, the following tests should be performed[70]: resting anal pressure, squeezing pressure,

Table 4 Interpretation of the manometric data

Test	Parameter evaluated	Interpretation
Resting pressure	IAS (70% of resting pressure) and EAS (30% of resting pressure)	*P* increased: Hypertonic sphincters (IAS and/or EAS). Oral nitroglycerin can identify the sphincter involved because it relaxes IAS, but not EAS
Squeeze pressure	EAS	The fatigue rate index can be calculated based on the pressure and duration of the contraction. However, the usefulness of the test in both constipated and incontinent patients is disputed[112,113]
Rectoanal inhibitory reflex	IAS relaxation during rectal inflation	Absent: Possible hirschsprung; If present with elevated volume inflation: Megarectum[57]
Rectal sensitivity	Rectal sensory function at different volumes	Elevated sensory thresholds may be linked to changes in rectal biomechanics (megarectum) or to afferent pathway dysfunction[114,115]
Rectal compliance	Mechanical rectal function	Increased compliance: megarectum[57]
Attempted defecation	Synchronisation between the increase in rectal pressure and the decrease in anal pressure during attempts to defecate	Three types of dysfunction may be detected[65]: Type 1: Adequate rectal *P* increase but associated with anal *P* increase; Type 2: Inadequate rectal *P* increase associated with anal *P* increase or inadequate anal *P* decrease; Type 3: Adequate rectal *P* increase but inadequate anal *P* decrease

IAS: Internal anal sphincter; EAS: External anal sphincter; *P*: Pressure. Modified from Azpiroz *et al*[57].

rectoanal inhibitory reflex, rectal sensations (first sensation, maximum tolerable volume), rectal compliance, and rectal and anal pressure during attempted defecation (straining)[57,71]. The results will vary with age and sex; normal values based on a large cohort of healthy individuals are still lacking[57]. Level Ⅲ evidence, Grade C recommendation.

How should I interpret the results of anorectal manometric tests for obstructed defecation? The interpretation of the manometric data in clinical and physiopathologic terms is summarised in Table 4.

Are there typical manometric abnormalities in chronic constipation and/or obstructed defecation? The main abnormality in obstructed defecation is absent or inadequate relaxation of the anal sphincter, sometimes associated, paradoxically, with contraction during straining (dyssynergia). Obstructed defecation may also be associated with absent or inadequate rectal pressure[65,67]. The "defecation index", or the ratio of maximal rectal pressure to minimal anal residual pressure[65], quantifies recto-anal coordination during attempted defecation. Abnormalities have also been reported in anal canal resting pressure, anal canal squeezing pressure (external anal sphincters exhaustion), rectoanal inhibitory reflex (RAIR), rectal sensitivity, and compliance. Level Ⅲ evidence, Grade C recommendation.

How can anorectal manometry be used to guide choices regarding therapy? Anorectal manometry can shed light on the physiopathologic mechanisms of obstructed defecation and help to develop a pelvic floor rehabilitation program for the patient[72]. It should be included in the pre-operative evaluation when a surgical reduction in rectal capacity is planned[73,74]. If RAIR is absent, Hirschsprung disease should be suspected. Elevated sensory thresholds, increased compliance, and rectal motor dysfunction are frequent in constipated patients[75,76] and can be treated with sensory retraining biofeedback therapy, based on sensory values obtained by means of anorectal manometry[77]. The results of biofeedback and electrical stimulation can be measured with anorectal manometry, and in fact, a reduction in rectal sensory thresholds has been demonstrated[78,79]. Level Ⅲ evidence, Grade C recommendation.

Balloon expulsion test

The balloon expulsion test is a simple, inexpensive test that can identify patients with abnormal defecation.

What is the usefulness of the balloon expulsion test to diagnose dyssynergic defecation? The balloon expulsion test has not yet been standardised; the filling volume of the balloon, the position of the patient, and the expulsion time have differed in various studies.

Trials including healthy controls. Two trials performed the test with the patient seated and the balloon filled with 50 mL of water; 59%[67] and 25%[80] of the constipated patients and 16%[67] of the controls were unable to expel the balloon within 5 min.

In the third trial[81], the expulsion time was not specified, and the test was performed with a balloon filled with different volumes of water; 100% of patients with idiopathic megarectum, 53% of patients with a normal colonic transit time, 36% of patients with a slow transit colonic time, and 7% of controls were unable to expel the balloon.

Other trials. Some trials[82-84] have assessed patients with pelvic floor dyssynergia and have reported positive results in 23% to 57% of patients. However, different methods were used, so the results are not comparable.

In one trial[85], the balloon was filled to the point at which the need to defecate was triggered, and the balloon had to be expelled within one minute. The authors concluded that a negative test is useful "to identify patients who do not have dyssynergia" and resulted in a specificity of 89%, a sensibility of 88%, a positive predictive value of 67%, and a negative predictive value of 97%.

The balloon expulsion test cannot be used as a gold standard for the diagnosis of "dyssynergic defecation" and should be integrated with other anorectal tests. Level

Ⅲ evidence, Grade C recommendation.

Colonic manometry

Slow transit constipation (STC) is characterised by prolonged colonic transit, generally measured in terms of intestinal transit time using radiopaque markers[86]. Colon manometry shows the daily patterns of bowel activity, identifying high amplitude waves, which correspond to mass movement in the intestine, and low amplitude waves[87,88]. Manometric studies[89,90] in STC patients have shown that propagating activity may be altered in frequency, amplitude and duration; segmental activity can be maintained or drastically lost, but there is, above all, a subversion of the periodicity of motor activity in the colon. Recently, a new method of evaluating propagated motor activity or "propagating sequences" has been developed, but it is still in the experimental stage[91].

What are the clinical applications of colonic manometry? In patients with serious STC symptoms, colonic manometry can be helpful in the diagnosis and in decisions regarding therapy (whether conservative or surgical)[61]. Level Ⅳ evidence, Grade C recommendation.

How should colon manometry be performed in patients with slow transit constipation? In the clinical setting, the bisacodyl test should be used. This procedure tests the stimulation of residual colonic propulsive activity, and it can be used to identify the subgroup of patients with severe slow transit constipation or "inertia coli", one incontrovertible indication for total colectomy[92-94]. Thus, colonic manometry may help to diagnose an underlying myopathy or neuropathy and to differentiate slower transit due to neuromuscular function[95]. Level Ⅴ evidence, Grade C recommendation.

Pathologies of the colon

The pathophysiology of slow transit constipation is not known[96], but there is evidence to indicate that certain subtypes of idiopathic constipation are secondary to visceral neuropathy[97-99], such as aberrant regulation of the nervous enteric system or parasympathetic alterations[100].

What STC alterations can be verified on histology? Qualitative and quantitative alterations in the enteric nervous system can be observed on histology, from alterations in the neurotransmitters to the loss of argyrophilic neurons and neurofilaments and myenteric plexus hypoganglionosis[101]. More recently, reductions in the number of cells of Cajal have been described[102,103]. Level Ⅲ evidence, Grade C recommendation.

Is an endoscopic biopsy sufficient, or is a full-wall thickness biopsy necessary? Endoscopic biopsies only provide information on the mucosa and cannot detect other histological alterations; therefore, they are not useful in the pathogenetic evaluation of STC. Given the nature of the alterations, it is necessary to conduct biopsies that reach the muscle layer.

What is the role of the suction biopsy in STC? Suction biopsy is the gold standard for the diagnosis of intestinal neurodysplasia, particularly in children. In the differential diagnosis, four biopsy samples should be taken between 2 cm and 10 cm from the pettinea linea[104]. The histological findings can distinguish STC from Hirschsprung disease and contribute to the diagnosis of intestinal neurodisplasia and other degenerative diseases of the colon (i.e., amyloidosis, desmosis, elastosis)[105]. Level Ⅱ evidence, Grade B recommendation.

What is the role of immunohistochemistry? Immunohistochemistry is the main tool for the histological evaluation of nerves and connective tissues. There are no clinical studies in the literature that focus on this particular examination. Pathologists recommend that immunohistochemical analysis be undertaken in suspected cases of STC[106].

The Consensus Committee therefore recommends that immunohistochemistry be performed to document patterns of slow transit constipation.

Gastrojejunal manometry

There is evidence that slow transit constipation subtends diffuse enteric neurological involvement, probably of the myenteric plexus and, above all, the system of interstitial cells of Cajal[107]. Various studies have highlighted different ileal dysfunctions: in two retrospective analyses, 20.6% of patients with chronic constipation showed gastrojejunal abnormalities[61,108]. Cardiovascular tests for dysautonomia, which are widely used in diabetic neuropathy, are not applicable in the diagnostic workup of slow transit constipation.

The most meaningful test for myopathic or neuropathic involvement (especially in the pre-surgical evaluation) in patients with chronic constipation is gastrojejunal manometry, as stated recently by the American Neurogastroenterology and Motility Society[109-111].

What are the clinical applications of gastrojejunal manometry? Gastrojejunal manometry can be used to analyse antro-duodenal activity and fasting jejunal motility, particularly in patients with autonomic dysfunctions, such as diabetic neuropathy. In a recent study of 61 subjects undergoing gastrojejunal manometry, all STC patients and 94% of those patients with normal transit constipation exhibited alterations in small bowel motility in the postprandial and fasting phases, but there were no significant differences between the two groups[109].

When should gastrojejunal manometry be performed in STC patients? In cases of STC, gastrojejunal manometry is recommended before surgery[93,109]. Level Ⅲ evidence, Grade C recommendation.

REFERENCES

1 An evidence-based approach to the management of chronic constipation in North America. *Am J Gastroenterol* 2005; **100** Suppl 1: S1-S4

2 **Wald A**. Constipation in the primary care setting: current concepts and misconceptions. *Am J Med* 2006; **119**: 736-739

3 **Longstreth GF**, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; **130**: 1480-1491

4 **Drossman DA**, Richter NJ, Talley NJ, Thompson WG,

Corazziari E, Whitehead WE. The functional gastrointestinal disorders: diagnosis, pathophysiology, and treatment. A multinational consensus. 1st ed. McLean, VA: Degnon Associates, 1994
5 **Thompson WG**, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Müller-Lissner SA. Functional bowel disorders and functional abdominal pain. *Gut* 1999; **45** Suppl 2: II43-II47
6 **O'Donnell LJ**, Virjee J, Heaton KW. Pseudo-diarrhoea in the irritable bowel syndrome: patients' records of stool form reflect transit time while stool frequency does not. *Gut* 1988; **29**: A1455
7 **Bharucha AE**, Wald A, Enck P, Rao S. Functional anorectal disorders. *Gastroenterology* 2006; **130**: 1510-1518
8 **Lenzi F**, Caniggia A. Manuale di semeiotica medica. Torino. *Edizioni Minerva Medica* 1969: 3-23
9 **Brandt LJ**, Prather CM, Quigley EM, Schiller LR, Schoenfeld P, Talley NJ. Systematic review on the management of chronic constipation in North America. *Am J Gastroenterol* 2005; **100** Suppl 1: S5-S21
10 **Whitehead WE**, Drinkwater D, Cheskin LJ, Heller BR, Schuster MM. Constipation in the elderly living at home. Definition, prevalence, and relationship to lifestyle and health status. *J Am Geriatr Soc* 1989; **37**: 423-429
11 **Lindberg G**, Hamid SS, Malfertheiner P, Thomsen OO, Fernandez LB, Garisch J, Thomson A, Goh KL, Tandon R, Fedail S, Wong BC, Khan AG, Krabshuis JH, LeMair A. World Gastroenterology Organisation global guideline: Constipation--a global perspective. *J Clin Gastroenterol* 2011; **45**: 483-487
12 **Beck DE**. Initial evaluation of constipation. In: Wexner SD, Bartolo DC, editors. Constipation evaluation and management. Oxford: Butterworth-Heinemann, 1995: 31-38
13 **Locke GR**, Pemberton JH, Phillips SF. AGA technical review on constipation. American Gastroenterological Association. *Gastroenterology* 2000; **119**: 1766-1778
14 **Mehra G**, Weekes A, Vantrappen P, Visvanathan D, Jeyarajah A. Laparoscopic assisted radical vaginal hysterectomy for cervical carcinoma: morbidity and long-term follow-up. *Eur J Surg Oncol* 2010; **36**: 304-308
15 **Murad-Regadas S**, Peterson TV, Pinto RA, Regadas FS, Sands DR, Wexner SD. Defecographic pelvic floor abnormalities in constipated patients: does mode of delivery matter? *Tech Coloproctol* 2009; **13**: 279-283
16 **Chatoor D**, Emmnauel A. Constipation and evacuation disorders. *Best Pract Res Clin Gastroenterol* 2009; **23**: 517-530
17 **Pare P**, Ferrazzi S, Thompson WG, Irvine EJ, Rance L. An epidemiological survey of constipation in canada: definitions, rates, demographics, and predictors of health care seeking. *Am J Gastroenterol* 2001; **96**: 3130-3137
18 **McCrea GL**, Miaskowski C, Stotts NA, Macera L, Varma MG. Pathophysiology of constipation in the older adult. *World J Gastroenterol* 2008; **14**: 2631-2638
19 **Bellini M**, Alduini P, Bassotti G, Bove A, Bocchini R, Sormani MP, Bruzzi P, Pucciani F. Self-perceived normality in defecation habits. *Dig Liver Dis* 2006; **38**: 103-108
20 **Pepin C**, Ladabaum U. The yield of lower endoscopy in patients with constipation: survey of a university hospital, a public county hospital, and a Veterans Administration medical center. *Gastrointest Endosc* 2002; **56**: 325-332
21 **Rex DK**, Lehman GA, Ulbright TM, Smith JJ, Pound DC, Hawes RH, Helper DJ, Wiersema MJ, Langefeld CD, Li W. Colonic neoplasia in asymptomatic persons with negative fecal occult blood tests: influence of age, gender, and family history. *Am J Gastroenterol* 1993; **88**: 825-831
22 **Altomare DF**, Rinaldi M, Martinelli E, Mitolo C. Grading the severity of chronic idiopathic constipation. *Tech Coloproctol* 1996; **1**: 27-28
23 **Frank L**, Kleinman L, Farup C, Taylor L, Miner P. Psychometric validation of a constipation symptom assessment questionnaire. *Scand J Gastroenterol* 1999; **34**: 870-877
24 **Agachan F**, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. *Dis Colon Rectum* 1996; **39**: 681-685
25 **Knowles CH**, Scott SM, Legg PE, Allison ME, Lunniss PJ. Level of classification performance of KESS (symptom scoring system for constipation) validated in a prospective series of 105 patients. *Dis Colon Rectum* 2002; **45**: 842-843
26 **Varma MG**, Wang JY, Berian JR, Patterson TR, McCrea GL, Hart SL. The constipation severity instrument: a validated measure. *Dis Colon Rectum* 2008; **51**: 162-172
27 **Altomare DF**, Spazzafumo L, Rinaldi M, Dodi G, Ghiselli R, Piloni V. Set-up and statistical validation of a new scoring system for obstructed defaecation syndrome. *Colorectal Dis* 2008; **10**: 84-88
28 **Eypasch E**, Williams JI, Wood-Dauphinee S, Ure BM, Schmülling C, Neugebauer E, Troidl H. Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. *Br J Surg* 1995; **82**: 216-222
29 **Marquis P**, De La Loge C, Dubois D, McDermott A, Chassany O. Development and validation of the Patient Assessment of Constipation Quality of Life questionnaire. *Scand J Gastroenterol* 2005; **40**: 540-551
30 **Wang JY**, Hart SL, Lee J, Berian JR, McCrea GL, Varma MG. A valid and reliable measure of constipation-related quality of life. *Dis Colon Rectum* 2009; **52**: 1434-1442
31 **Hinton JM**, Lennard-Jones JE, Young AC. A ne method for studying gut transit times using radioopaque markers. *Gut* 1969; **10**: 842-847
32 **Metcalf AM**, Phillips SF, Zinsmeister AR, MacCarty RL, Beart RW, Wolff BG. Simplified assessment of segmental colonic transit. *Gastroenterology* 1987; **92**: 40-47
33 **Bartram CI**, Turnbull GK, Lennard-Jones JE. Evacuation proctography: an investigation of rectal expulsion in 20 subjects without defecatory disturbance. *Gastrointest Radiol* 1988; **13**: 72-80
34 **Altringer WE**, Saclarides TJ, Dominguez JM, Brubaker LT, Smith CS. Four-contrast defecography: pelvic "floor-oscopy". *Dis Colon Rectum* 1995; **38**: 695-699
35 **Maglinte DD**, Kelvin FM, Hale DS, Benson JT. Dynamic cystoproctography: a unifying diagnostic approach to pelvic floor and anorectal dysfunction. *AJR Am J Roentgenol* 1997; **169**: 759-767
36 **Lienemann A**, Anthuber C, Baron A, Kohz P, Reiser M. Dynamic MR colpocystorectography assessing pelvic-floor descent. *Eur Radiol* 1997; **7**: 1309-1317
37 **Beer-Gabel M**, Teshler M, Barzilai N, Lurie Y, Malnick S, Bass D, Zbar A. Dynamic transperineal ultrasound in the diagnosis of pelvic floor disorders: pilot study. *Dis Colon Rectum* 2002; **45**: 239-245; discussion 245-248
38 **Beer-Gabel M**, Teshler M, Schechtman E, Zbar AP. Dynamic transperineal ultrasound vs. defecography in patients with evacuatory difficulty: a pilot study. *Int J Colorectal Dis* 2004; **19**: 60-67
39 **Dietz HP**, Steensma AB. Posterior compartment prolapse on two-dimensional and three-dimensional pelvic floor ultrasound: the distinction between true rectocele, perineal hypermobility and enterocele. *Ultrasound Obstet Gynecol* 2005; **26**: 73-77
40 **Brusciano L**, Limongelli P, Pescatori M, Napolitano V, Gagliardi G, Maffettone V, Rossetti G, del Genio G, Russo G, Pizza F, del Genio A. Ultrasonographic patterns in patients with obstructed defaecation. *Int J Colorectal Dis* 2007; **22**: 969-977
41 **Kuijpers HC**, Bleijenberg G, de Morree H. The spastic pelvic floor syndrome. Large bowel outlet obstruction caused by pelvic floor dysfunction: a radiological study. *Int J Colorectal Dis* 1986; **1**: 44-48
42 **Halligan S**, Bartram CI, Park HJ, Kamm MA. Proctographic

features of anismus. *Radiology* 1995; **197**: 679-682
43 **Maglinte DD**, Kelvin FM, Fitzgerald K, Hale DS, Benson JT. Association of compartment defects in pelvic floor dysfunction. *AJR Am J Roentgenol* 1999; **172**: 439-444
44 **Ott DJ**, Donati DL, Kerr RM, Chen MY. Defecography: results in 55 patients and impact on clinical management. *Abdom Imaging* 1994; **19**: 349-354
45 **Hiltunen KM**, Kolehmainen H, Matikainen M. Does defecography help in diagnosis and clinical decision-making in defecation disorders? *Abdom Imaging* 1994; **19**: 355-358
46 **Spazzafumo L**, Piloni V. Rectal constipation and clinical decision-making: multiple correspondence analysis of defecographic findings. *Tech Coloproctol* 1999; **3**: 117-121
47 **Healy JC**, Halligan S, Reznek RH, Watson S, Bartram CI, Phillips R, Armstrong P. Dynamic MR imaging compared with evacuation proctography when evaluating anorectal configuration and pelvic floor movement. *AJR Am J Roentgenol* 1997; **169**: 775-779
48 **Kelvin FM**, Maglinte DD, Hale DS, Benson JT. Female pelvic organ prolapse: a comparison of triphasic dynamic MR imaging and triphasic fluoroscopic cystocolpoproctography. *AJR Am J Roentgenol* 2000; **174**: 81-88
49 **Filler AG**. Diagnosis and management of pudendal nerve entrapment syndromes: impact of MR neurography and open MR-guided injections. *Neurosurg Q* 2008; **18**: 1-6
50 **Sultan AH**, Loder PB, Bartram CI, Kamm MA, Hudson CN. Vaginal endosonography. New approach to image the undisturbed anal sphincter. *Dis Colon Rectum* 1994; **37**: 1296-1299
51 **Halligan S**, Northover J, Bartram CI. Vaginal endosonography to diagnose enterocoele. *Br J Radiol* 1996; **69**: 996-999
52 **Gold DM**, Bartram CI, Halligan S, Humphries KN, Kamm MA, Kmiot WA. Three-dimensional endoanal sonography in assessing anal canal injury. *Br J Surg* 1999; **86**: 365-370
53 **Dietz HP**. Ultrasound imaging of the pelvic floor. Part I: two-dimensional aspects. *Ultrasound Obstet Gynecol* 2004; **23**: 80-92
54 **Dietz HP**. Ultrasound imaging of the pelvic floor. Part II: three-dimensional or volume imaging. *Ultrasound Obstet Gynecol* 2004; **23**: 615-625
55 **Santoro GA**, Fortling B. The advantages of volume rendering in three-dimensional endosonography of the anorectum. *Dis Colon Rectum* 2007; **50**: 359-368
56 **Piloni V**, Spazzafumo L. Evacuation sonography. *Tech Coloproctol* 2005; **9**: 119-125; discussion 125-126
57 **Azpiroz F**, Enck P, Whitehead WE. Anorectal functional testing: review of collective experience. *Am J Gastroenterol* 2002; **97**: 232-240
58 **Schizas AM**, Emmanuel AV, Williams AB. Anal canal vector volume manometry. *Dis Colon Rectum* 2011; **54**: 759-768
59 **Jones MP**, Post J, Crowell MD. High-resolution manometry in the evaluation of anorectal disorders: a simultaneous comparison with water-perfused manometry. *Am J Gastroenterol* 2007; **102**: 850-855
60 **Bharucha AE**, Seide B, Fox JC, Zinsmeister AR. Day-to-day reproducibility of anorectal sensorimotor assessments in healthy subjects. *Neurogastroenterol Motil* 2004; **16**: 241-250
61 **Camilleri M**, Bharucha AE, di Lorenzo C, Hasler WL, Prather CM, Rao SS, Wald A. American Neurogastroenterology and Motility Society consensus statement on intraluminal measurement of gastrointestinal and colonic motility in clinical practice. *Neurogastroenterol Motil* 2008; **20**: 1269-1282
62 **Rao SS**. A balancing view: Fecal incontinence: test or treat empirically--which strategy is best? *Am J Gastroenterol* 2006; **101**: 2683-2684
63 **Corsetti M**, Passaretti S, Barzaghi F, Limido E, Bottini C, Tessera G, Gianfrate L, Bonecco S, Noris RA, Castagna V, Radaelli F, Strocchi E, Dinelli M, Fossati D, Strada E, Viviani G, Casa DD, Missale G. Gruppo Lombardo per lo Studio della Motilità Intestinale. Anorectal manometry with water-perfused catheter in healthy adults with no functional bowel disorders. *Colorectal Dis* 2010; **12**: 220-225
64 **Gundling F**, Seidl H, Scalercio N, Schmidt T, Schepp W, Pehl C. Influence of gender and age on anorectal function: normal values from anorectal manometry in a large caucasian population. *Digestion* 2010; **81**: 207-213
65 **Sun WM**, Rao SS. Manometric assessment of anorectal function. *Gastroenterol Clin North Am* 2001; **30**: 15-32
66 **Rao SS**. Constipation: evaluation and treatment of colonic and anorectal motility disorders. *Gastrointest Endosc Clin N Am* 2009; **19**: 117-139, vii
67 **Rao SS**, Welcher KD, Leistikow JS. Obstructive defecation: a failure of rectoanal coordination. *Am J Gastroenterol* 1998; **93**: 1042-1050
68 **Wald A**. Clinical practice. Fecal incontinence in adults. *N Engl J Med* 2007; **356**: 1648-1655
69 **Pehl C**, Schmidt T, Schepp W. Slow transit constipation: more than one disease? *Gut* 2002; **51**: 610; author reply 610
70 **Rao SS**, Azpiroz F, Diamant N, Enck P, Tougas G, Wald A. Minimum standards of anorectal manometry. *Neurogastroenterol Motil* 2002; **14**: 553-559
71 **Bharucha AE**. Update of tests of colon and rectal structure and function. *J Clin Gastroenterol* 2006; **40**: 96-103
72 **Pucciani F**, Rottoli ML, Bologna A, Cianchi F, Forconi S, Cutellè M, Cortesini C. Pelvic floor dyssynergia and bimodal rehabilitation: results of combined pelviperineal kinesitherapy and biofeedback training. *Int J Colorectal Dis* 1998; **13**: 124-130
73 **Gearhart S**, Hull T, Floruta C, Schroeder T, Hammel J. Anal manometric parameters: predictors of outcome following anal sphincter repair? *J Gastrointest Surg* 2005; **9**: 115-120
74 **Glasgow SC**, Birnbaum EH, Kodner IJ, Fleshman JW, Dietz DW. Preoperative anal manometry predicts continence after perineal proctectomy for rectal prolapse. *Dis Colon Rectum* 2006; **49**: 1052-1058
75 **Gladman MA**, Scott SM, Chan CL, Williams NS, Lunniss PJ. Rectal hyposensitivity: prevalence and clinical impact in patients with intractable constipation and fecal incontinence. *Dis Colon Rectum* 2003; **46**: 238-246
76 **Scott SM**, van den Berg MM, Benninga MA. Rectal sensorimotor dysfunction in constipation. *Best Pract Res Clin Gastroenterol* 2011; **25**: 103-118
77 **Gladman MA**, Lunniss PJ, Scott SM, Swash M. Rectal hyposensitivity. *Am J Gastroenterol* 2006; **101**: 1140-1151
78 **Battaglia E**, Serra AM, Buonafede G, Dughera L, Chistolini F, Morelli A, Emanuelli G, Bassotti G. Long-term study on the effects of visual biofeedback and muscle training as a therapeutic modality in pelvic floor dyssynergia and slow-transit constipation. *Dis Colon Rectum* 2004; **47**: 90-95
79 **Chang HS**, Myung SJ, Yang SK, Jung HY, Kim TH, Yoon IJ, Kwon OR, Hong WS, Kim JH, Min YI. Effect of electrical stimulation in constipated patients with impaired rectal sensation. *Int J Colorectal Dis* 2003; **18**: 433-438
80 **Bannister JJ**, Timms JM, Barfield LJ, Donnelly TC, Read NW. Physiological studies in young women with chronic constipation. *Int J Colorectal Dis* 1986; **1**: 175-182
81 **Barnes PR**, Lennard-Jones JE. Balloon expulsion from the rectum in constipation of different types. *Gut* 1985; **26**: 1049-1052
82 **Fleshman JW**, Dreznik Z, Cohen E, Fry RD, Kodner IJ. Balloon expulsion test facilitates diagnosis of pelvic floor outlet obstruction due to nonrelaxing puborectalis muscle. *Dis Colon Rectum* 1992; **35**: 1019-1025
83 **Glia A**, Lindberg G, Nilsson LH, Mihocsa L, Akerlund JE. Constipation assessed on the basis of colorectal physiology. *Scand J Gastroenterol* 1998; **33**: 1273-1279
84 **Rao SS**, Mudipalli RS, Stessman M, Zimmerman B. Investigation of the utility of colorectal function tests and Rome II criteria in dyssynergic defecation (Anismus). *Neurogastroenterol Motil* 2004; **16**: 589-596

85 **Minguez M**, Herreros B, Sanchiz V, Hernandez V, Almela P, Añon R, Mora F, Benages A. Predictive value of the balloon expulsion test for excluding the diagnosis of pelvic floor dyssynergia in constipation. *Gastroenterology* 2004; **126**: 57-62

86 **Lembo A**, Camilleri M. Chronic constipation. *N Engl J Med* 2003; **349**: 1360-1368

87 **Bassotti G**, Germani U, Morelli A. Human colonic motility: physiological aspects. *Int J Colorectal Dis* 1995; **10**: 173-180

88 **Bassotti G**. The response of the human colon to food ingestion. *Diabetes Nutr Metab* 1990; **3**: 91-94

89 **Bassotti G**, Iantorno G, Fiorella S, Bustos-Fernandez L, Bilder CR. Colonic motility in man: features in normal subjects and in patients with chronic idiopathic constipation. *Am J Gastroenterol* 1999; **94**: 1760-1770

90 **Rao SS**, Sadeghi P, Beaty J, Kavlock R. Ambulatory 24-hour colonic manometry in slow-transit constipation. *Am J Gastroenterol* 2004; **99**: 2405-2416

91 **Dinning PG**, Szczesniak MM, Cook IJ. Twenty-four hour spatiotemporal mapping of colonic propagating sequences provides pathophysiological insight into constipation. *Neurogastroenterol Motil* 2008; **20**: 1017-1021

92 **Bassotti G**, Chistolini F, Nzepa FS, Morelli A. Colonic propulsive impairment in intractable slow-transit constipation. *Arch Surg* 2003; **138**: 1302-1304

93 **Bassotti G**, Roberto GD, Sediari L, Morelli A. Toward a definition of colonic inertia. *World J Gastroenterol* 2004; **10**: 2465-2467

94 **Rao SS**, Singh S. Clinical utility of colonic and anorectal manometry in chronic constipation. *J Clin Gastroenterol* 2010; **44**: 597-609

95 **Rao SS**, Meduri K. What is necessary to diagnose constipation? *Best Pract Res Clin Gastroenterol* 2011; **25**: 127-140

96 **Zarate N**, Knowles CH, Newell M, Garvie NW, Gladman MA, Lunniss PJ, Scott SM. In patients with slow transit constipation, the pattern of colonic transit delay does not differentiate between those with and without impaired rectal evacuation. *Am J Gastroenterol* 2008; **103**: 427-434

97 **Bassotti G**, De Giorgio R, Stanghellini V, Tonini M, Barbara G, Salvioli B, Fiorella S, Corinaldesi R. Constipation: a common problem in patients with neurological abnormalities. *Ital J Gastroenterol Hepatol* 1998; **30**: 542-548

98 **Mitolo-Chieppa D**, Mansi G, Nacci C, De Salvia MA, Montagnani M, Potenza MA, Rinaldi R, Lerro G, Siro-Brigiani G, Mitolo CI, Rinaldi M, Altomare DF, Memeo V. Idiopathic chronic constipation: tachykinins as cotransmitters in colonic contraction. *Eur J Clin Invest* 2001; **31**: 349-355

99 **Penning C**, Steens J, van der Schaar PJ, Kuyvenhoven J, Delemarre JB, Lamers CB, Masclee AA. Motor and sensory function of the rectum in different subtypes of constipation. *Scand J Gastroenterol* 2001; **36**: 32-38

100 **Knowles CH**, Scott SM, Lunniss PJ. Slow transit constipation: a disorder of pelvic autonomic nerves? *Dig Dis Sci* 2001; **46**: 389-401

101 **Faussone-Pellegrini MS**, Infantino A, Matini P, Masin A, Mayer B, Lise M. Neuronal anomalies and normal muscle morphology at the hypomotile ileocecocolonic region of patients affected by idiopathic chronic constipation. *Histol Histopathol* 1999; **14**: 1119-1134

102 **He CL**, Burgart L, Wang L, Pemberton J, Young-Fadok T, Szurszewski J, Farrugia G. Decreased interstitial cell of cajal volume in patients with slow-transit constipation. *Gastroenterology* 2000; **118**: 14-21

103 **Bassotti G**, Villanacci V, Maurer CA, Fisogni S, Di Fabio F, Cadei M, Morelli A, Panagiotis T, Cathomas G, Salerni B. The role of glial cells and apoptosis of enteric neurones in the neuropathology of intractable slow transit constipation. *Gut* 2006; **55**: 41-46

104 **Martucciello G**, Pini Prato A, Puri P, Holschneider AM, Meier-Ruge W, Jasonni V, Tovar JA, Grosfeld JL. Controversies concerning diagnostic guidelines for anomalies of the enteric nervous system: a report from the fourth International Symposium on Hirschsprung's disease and related neurocristopathies. *J Pediatr Surg* 2005; **40**: 1527-1531

105 **Pini-Prato A**, Avanzini S, Gentilino V, Martucciello G, Mattioli G, Coccia C, Parodi S, Bisio GM, Jasonni V. Rectal suction biopsy in the workup of childhood chronic constipation: indications and diagnostic value. *Pediatr Surg Int* 2007; **23**: 117-122

106 **Vanderwinden JM**, Rumessen JJ. Interstitial cells of Cajal in human gut and gastrointestinal disease. *Microsc Res Tech* 1999; **47**: 344-360

107 **Bassotti G**, Stanghellini V, Chiarioni G, Germani U, De Giorgio R, Vantini I, Morelli A, Corinaldesi R. Upper gastrointestinal motor activity in patients with slow-transit constipation. Further evidence for an enteric neuropathy. *Dig Dis Sci* 1996; **41**: 1999-2005

108 **Penning C**, Vu MK, Delemarre JB, Masclee AA. Proximal gastric motor and sensory function in slow transit constipation. *Scand J Gastroenterol* 2001; **36**: 1267-1273

109 **Seidl H**, Gundling F, Pehl C, Pfeiffer A, Schepp W, Schmidt T. Small bowel motility in functional chronic constipation. *Neurogastroenterol Motil* 2009; **21**: 1278-e122

110 **Stanghellini V**, Cogliandro R, Cogliandro L, De Giorgio R, Barbara G, Salvioli B, Corinaldesi R. Clinical use of manometry for the diagnosis of intestinal motor abnormalities. *Dig Liver Dis* 2000; **32**: 532-541

111 **Altomare DF**, Portincasa P, Rinaldi M, Di Ciaula A, Martinelli E, Amoruso A, Palasciano G, Memeo V. Slow-transit constipation: solitary symptom of a systemic gastrointestinal disease. *Dis Colon Rectum* 1999; **42**: 231-240

112 **Marcello PW**, Barrett RC, Coller JA, Schoetz DJ, Roberts PL, Murray JJ, Rusin LC. Fatigue rate index as a new measurement of external sphincter function. *Dis Colon Rectum* 1998; **41**: 336-343

113 **Bilali S**, Pfeifer J. Anorectal manometry: are fatigue rate and fatigue rate index of any clinical importance? *Tech Coloproctol* 2005; **9**: 225-228

114 **Gladman MA**, Dvorkin LS, Lunniss PJ, Williams NS, Scott SM. Rectal hyposensitivity: a disorder of the rectal wall or the afferent pathway? An assessment using the barostat. *Am J Gastroenterol* 2005; **100**: 106-114

115 **Gladman MA**, Aziz Q, Scott SM, Williams NS, Lunniss PJ. Rectal hyposensitivity: pathophysiological mechanisms. *Neurogastroenterol Motil* 2009; **21**: 508-516, e4-5

S- Editor Yang XC **L- Editor** A **E- Editor** Li JY