



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

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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.

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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,

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

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.

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.

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^[5-5].

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

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

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 greater 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)	<i>P</i> 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 <i>P</i> increase but associated with anal <i>P</i> increase; Type 2: Inadequate rectal <i>P</i> increase associated with anal <i>P</i> increase or inadequate anal <i>P</i> decrease; Type 3: Adequate rectal <i>P</i> increase but inadequate anal <i>P</i> 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 bio-

feedback 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 pectinea line^[104]. The histological findings can distinguish STC from Hirschsprung disease and contribute to the diagnosis of intestinal neurodysplasia 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 neuro-pathic 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.

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