



Universidade do Minho
Escola de Medicina

Ana Célia Caetano

**The role of low-cost strategies in the
evaluation of defecation disorders**



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Trabalho Efetuado sob a orientação da
Professora Carla Rolanda
e do
Professor Jorge Correia-Pinto

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À minha orientadora e amiga. Por nunca ter desistido de mim.

A todos os que me ajudaram ao longo deste percurso.

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Dedicatória

Aos meus filhos Tiago, Filipe e Maria.

Ao meu Marido.

Aos meus Pais e à minha Irmã.

Pelo vosso Amor incondicional.

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O papel das estratégias de baixo custo na avaliação dos distúrbios evacuatórios

RESUMO

Objectivos: Pretende-se com este trabalho, através de uma descrição epidemiológica da obstipação crónica, identificar factores e comportamentos potencialmente modificáveis na nossa população. Pretende-se também avaliar o papel de técnicas de baixo custo no rastreio de distúrbios evacuatórios nos doentes obstipados.

Métodos: Foi realizado um inquérito epidemiológico transversal na população de Braga que incluiu os hábitos intestinais e possíveis aspectos relacionados. Os doentes obstipados do nosso hospital terciário foram avaliados prospectivamente com técnicas de baixo custo (score clínico, score de toque rectal e teste de expulsão de balão), além de submetidos à avaliação fisiológica anorectal convencional.

Resultados: O inquérito epidemiológico analisou 1335 indivíduos. A prevalência da obstipação crónica foi 17,8%. Os doentes obstipados eram mais jovens (OR 1.01; 95% CI, 1.007-1.031), sós (OR 2.48; 95% CI, 1.7-3.47) e com baixo rendimento (OR 2.40; 95% CI, 1.77-3.47). Além disso, os doentes obstipados descreveram uma evacuação prolongada ($p=0.001$) e comportamentos específicos na casa-de-banho como ausência de padrão matinal ($p=0.008$), recurso a factores desencadeantes ($p=0.001$) e a material de leitura/tecnológico ($p=0.006$) para facilitar a evacuação. O estudo prospectivo avaliou 98 doentes obstipados (38,9% com distúrbios evacuatórios). O teste de balão sequencial com volume variável (associado a vontade constante de evacuar), seguido pelo teste de expulsão de balão convencional (com volume fixo), melhorou a performance desta técnica no rastreio dos distúrbios defecatórios, com uma sensibilidade de 86%, especificidade de 67% e valor preditivo negativo de 87%.

Discussão e Conclusão: A obstipação crónica afecta 1 em cada 5 Portugueses que desenvolvem um perfil específico de hábitos evacuatórios. Embora o score clínico e o toque rectal não tenham revelado poder discriminatório suficiente, ao mudar a técnica de expulsão de balão, adicionamos a avaliação sensorial ao teste e melhorámos a sua performance no rastreio de distúrbios defecatórios.

Palavras-chave: obstipação crónica, distúrbios evacuatórios, teste de expulsão de balão, comportamentos evacuatórios.

The role of low-cost strategies in the evaluation of defecation disorders

ABSTRACT

Aims: We intend to analyse factors and behaviours related to chronic constipation in the local community. We also plan to evaluate the performance of low-cost tools for screening for defecation disorders in constipated patients.

Methods: A cross-sectional epidemiological survey regarding bowel habits in the general community of Braga was conducted. Besides, constipated patients of our tertiary hospital were prospectively assessed by low-cost tools (clinical score, digital rectal examination score and balloon expulsion test), besides the gold standard anorectal physiological evaluation.

Results: Regarding the survey, 1335 questionnaires were analysed. The prevalence of chronic constipation was 17,8%. This condition was more likely in younger (OR 1.01; 95% CI, 1.007-1.031), solo (OR 2.48; 95% CI, 1.7-3.47) and low-income (OR 2.40; 95% CI, 1.77-3.47) individuals. Constipated individuals spent more time at defecation ($p=0.001$) and have specific toilet behaviours as the absence of morning pattern ($p=0.008$), the use of triggers ($p=0.001$) and reading/technological material ($p=0.006$) to facilitate the evacuation. The prospective study evaluated 98 constipated patients (38,9% with a defecation disorder). A sequential balloon expulsion test with a variable volume (associated with a constant desire to evacuate) followed by the standard fixed volume balloon expulsion test improved the performance of the technique, with a sensitivity of 86%, specificity of 67% and a negative predictive value of 87%. The sequential balloon expulsion test had an OR 8.942, $p > 0.001$, CI 3.18-25.14, revealing to be the most significant predictor for defecation disorders screening.

Discussion and Conclusions: Chronic constipation affects 1 in each 5 Portuguese. Constipated patients are younger, solo and with low-income. They develop a clear toilet behaviour profile. By changing the technique of the balloon expulsion test, we allowed the evaluation of rectal sensory and improved the performance of this low-cost tool making it a more effective screening tool for defecation disorders.

Key-words: chronic constipation, defecation disorders, balloon expulsion test, toilet behaviours.

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ABBREVIATIONS

A

ARM - anorectal manometry

AUC – area under the curve

B

BET - balloon expulsion test

BSFS – Bristol stool form scale

C

CC – chronic constipation

COSMIN - COnsensus-based Standards for the selection of health status Measurement INstruments

CTT - Colon transit time

D

DD(s) – defecation disorder(s)

DEF – defecography

DGBI(s) - Disorders of Gut-Brain Interaction

DRE – digital rectal examination

DRESS – digital rectal examination scoring system

E

EMG – electromyography

F

FC – functional constipation

FGID(s) - Functional Gastrointestinal Disorder(s)

H

HRM – high resolution manometry

I

IBS-C – irritable bowel syndrome – subtype constipation

M

MR - magnetic resonance

N

NPV – negative predictive value

NSAIDs - Non-steroidal anti- inflammatory drugs

P

PPV – positive predictive value

R

ROC - Receiver Operating Characteristic

S

sBET – standard balloon expulsion test

V

wBET – variable volume balloon expulsion test

PART 1.

INTRODUCTION

CHAPTER 1. GENERAL INTRODUCTION

1.1 Walk through the clinical concepts

A defecation disorder (DD) is defined as a difficulty in evacuation or emptying the rectum. (Bharucha & Rao 2014) The DD may result from disordered anorectal function or structural anorectal disturbances, exemplified in Table 1. These pathophysiological mechanisms may often coexist. (Rao et al. 1998) (Gadman et al. 2006; Chiarioni G et al. 2005) Most complains of these patients fit into chronic constipation (CC). (Bharucha & Lacy 2020; Bharucha et al. 2013)

Table 1 - Mechanisms of defecation disorders

Inadequate rectal propulsion	Rectocele
Impaired anal relaxation or paradoxical contraction	Rectal prolapse
Rectal hyposensitivity	Intussusception
Anal hypersensitivity	Enterocoele
Perineal laxity	Sigmoidocoele
	Peritoneocoele

CC is a symptom-based disorder that includes a broad set of complaints as decreased stool frequency, straining, incomplete evacuation and sense of anorectal blockage for more than 3 months. CC is either a secondary condition (due to other diseases, medications or anatomic alterations as described in Table 2) or, more frequently, a primary disorder - related to neuromuscular or sensory-motor dysfunction. (Bharucha & Lacy 2020)

Table 2 - Secondary causes of constipation

<u>Endocrine conditions</u>	<u>Mechanical abnormalities</u>	<u>Medication</u>
Diabetes Mellitus	Colonic strictures	Opioids
Hypothyroidism	Colon and rectal cancer	Anticholinergic
Hypercalcemia	Inflammatory bowel disease	Iron supplements
<u>Myopathic conditions</u>	<u>Neurologic conditions</u>	Tricyclic antidepressants
Amyloidosis	Parkinson disease	Antipsychotics
Scleroderma	Multiple sclerosis	Calcium channel blockers
	Cerebrovascular disease	Anti-histamines
<u>Others</u>		NSAIDs
Immobility		Diuretics
Pregnancy		

Primary disorders of the digestive system can be diagnosed using the Rome criteria. (<https://theromefoundation.org/>) The Rome Foundation is a non-profit organization established in 1996 that supports the creation of scientific data and educational information regarding the Disorders of Gut-Brain Interaction (DGBIs) previously called the Functional Gastrointestinal Disorders (FGIDs). (Schmulson & Drossman 2017; Drossman 2016) Over the last 25 years, the Rome Foundation classified, critically reviewed and updated the scientific information regarding DGBIs, making recommendations for their diagnosis and treatment with great impact in clinical practice and research.

The Rome IV criteria (Aziz et al. 2020; Simren et al. 2017) provide a symptom-based definition of CC and recognise subgroups of CC based on both symptoms and objective physiological criteria. Rome criteria IV update regarding CC, accommodates both functional constipation (FC) and irritable bowel syndrome – subtype constipation (IBS-C) as part of a continuum spectrum of CC (Table 3). Based on evidence that shows substantial symptom overlap among the different pathophysiological entities of CC, (Rao et al. 2004; Halverson & Orkin 1998) Rome IV criteria state the need of anorectal tests to substantiate the diagnosis of DD among constipated patients. (Simren et al. 2017) According to the Rome IV criteria, the diagnosis of DD (Table 3) is established when a constipated patient has an impaired evacuation, demonstrated by 2 of 3 types of tests – balloon expulsion test (BET); dynamic anorectal image (conventional defecography, dynamic magnetic resonance or dynamic ultrasound); anorectal manometry (ARM) or electromyography (EMG). An extensive technical description of these tests is made elsewhere (Bharucha et al. 2013) but a brief description can be found in the section 1.3 of this Introduction.

Table 3 - Rome IV criteria for constipation and defecation disorders

Diagnostic Criteria (a) for Functional Constipation

1. Must include 2 or more of the following:
 - a. Straining during more than one-fourth (25%) of defecations
 - b. Lumpy or hard stools (BSFS 1-2) more than one-fourth (25%) of defecations
 - c. Sensation of incomplete evacuation more than one-fourth (25%) of defecations
 - d. Sensation of anorectal obstruction more than one-fourth (25%) of defecations
 - e. Manual manoeuvres to facilitate more than one fourth (25%) of defecations
 - f. Fewer than 3 spontaneous bowel movements per week
 2. Loose stools are rarely present without the use of laxatives
 3. Insufficient criteria for irritable bowel syndrome
-

Diagnostic Criteria (a) for irritable bowel syndrome with constipation

1. Recurrent abdominal pain at least one day a week with 2 or more of the following:
 - a. Related to defecation
 - b. Related to change in frequency of stools
 - c. Related to change in form of stools
 2. Lumpy or hard stools (BSFS 1-2) more than one-fourth (25%) of defecations
-

Diagnostic Criteria (a) for Functional Defecation Disorders

1. The patient must satisfy diagnostic criteria for functional constipation and/or irritable bowel syndrome with constipation
 2. During repeated attempts to defecate, there must be features of impaired evacuation, as demonstrated by 2 of the following 3 tests:
 - a. Abnormal balloon expulsion test
 - b. Abnormal anorectal evacuation pattern with manometry or anal surface EMG
 - c. Impaired rectal evacuation by imaging
-

(a) Criteria fulfilled for the last 3 months, symptom onset 6 months before diagnosis.

BSFS (Bristol Stool Form Scale)

(Adapted from Simren et al. 2017)

1.2 Exploring the Epidemiology

CC is one of the most frequent gastrointestinal diagnoses made in ambulatory medicine. In addition to its high prevalence, the economic cost and adverse implications on the quality of life make CC a major public health condition. (Bharucha & Lacy 2020; Bharucha & Wald 2019; Dik et al. 2014) The worldwide prevalence of CC among adults is estimated to be around 15% but this prevalence varies widely, ranging from 0.7% to 79%. (Mugie et al. 2011; Soares & Ford 2011; Peppas et al. 2008) One important aspect that may contribute to the prevalence variation is the difference in the methodology and definition of constipation in each study. (Werth et al. 2019; Siproudhis et al. 2006) Many of the community surveys used either self-report constipation or questionnaires based on one or some of the symptoms described in previous iterations of the Rome criteria. (Werth et

al. 2019; Soares & Ford 2011) This wide variation may also be explained by differences in populations like age, culture, diet and environment. (Werth et al. 2019; Siproudhis et al. 2006) Several other factors as physical activity, socioeconomic level, psychological parameters and vaginal delivery are frequently implicated in CC but also with various discrepancies (Bharucha & Lacy 2020; Higgins & Johanson 2004; Bytzer et al. 2001) For instance, regarding dietary habits, there are data suggesting that the Mediterranean diet (MD) might be beneficial in ameliorating functional gastrointestinal symptoms in children and adolescents (Agakidis et al. 2019) but there is no information regarding adult population. Besides the burden, only a minority of patients, seek specific medical advice, making the information regarding toilet behaviours, self-management and healthcare use scarce and not well understood. (Jones & Ballard 2008; Gálvez et al. 2006) Lastly, DDs account for around half of all constipated patients, according to a recent meta-analysis. (Vidlock et al. 2013) Vidlock *et al*/reviewed 79 studies including 7591 constipated patients and a DD was identified in 47,7% of patients evaluated by anorectal manometry and in 52,9% of patients evaluated by anal ultrasonography. These numbers illustrate the significant weight of DD in constipated patients.

1.3 The algorithmic approach of CC

As constipation is commonly reported to the family doctor and other healthcare professionals, the regular approach includes several general steps. (Bharucha & Lacy 2020; Simren et al. 2017) A meticulous clinical history should include evaluation of potential co-morbidities and medications causing secondary constipation (highlighted in Table 2). A physical exam including a proctological examination is also essential to identify potential abdominal or anorectal mass. (Talley 2008) Basic analysis can exclude anemia, celiac disease, thyroid alterations or ionic imbalance. At this point, alarm symptoms or signs are surely excluded and a primary disorder is commonly considered. The initial management approach of constipated patients focuses on diet and lifestyle modifications (increased fiber intake and physical activity, reduced stress, toileting in familiar surroundings). If patients experience difficulty in expelling stool, they should be advised to place a support approximately 6 inches in height under their feet when sitting on a toilet so that the hips are flexed toward a squatting posture. (Bharucha & Rao 2014; Sakakibara et al 2010) These diet and lifestyle modifications are generally healthy measures but the evidence that they improve constipation is scarce and the practical results frequently disappointing. The next step includes laxatives as appropriate, with an empiric management of diverse combinations being a true juggling. In patients

who do not respond to over-the-counter laxatives, it's the time to refer to the expert. At this point, there are still a large number of unsatisfied constipated patients, if we consider the high prevalence of the CC and the fact that around half are non-diagnosed DD. DD management approach shifts in other direction that includes biofeedback therapy, electrostimulation, specify pelvic floor surgical interventions. (Bharucha & Lacy 2020; Bharucha et al. 2013)

By other side, intestinal secretagogues and/or prokinetic agents may be recommended to non-DD constipated patients. Peripherally acting μ -opiate antagonists are another option for opioid-induced constipation. For specific refractory constipated patients, invasive measures can be at the table, including sacral nerve stimulation, colectomy or other surgical options. The guidance for individualized treatment and management of refractory patients are a truly clinical challenge.

1.4 Uncovering anorectal evaluation

As stated, CC is a symptom-based disorder but the diagnosis of DD in constipated individuals needs both symptoms and objective physiological criteria. (Simren et al. 2017) Several anorectal physiological tests were developed to evaluate and to classify patients' constipation. (Noelting et al. 2016) These tests are performed in tertiary centres that aggregates these specific exams and consultations in Anorectal Physiological Units.

BET technique – this is a simple procedure, first described by Preston and Lennard-Jones that evaluates a patient's ability to evacuate a filled balloon. (Preston & Lennard-Jones 1985) Most centres use a regular or commercial balloon. Different methodologies consider air or water filled balloon and the lying or seated position to perform the BET. Recommended time values range from less than 1 minute to up to 5 minutes. (Noelting et al. 2012)

Dynamic anorectal image (conventional defecography, dynamic MR and dynamic anorectal ultrasound) – in this type of exam, dynamically images of the rectum and pelvic floor are obtained during attempted defecation. It can detect structural abnormalities such as a rectocele or rectal prolapse, and it can also identify functional parameters such as the anorectal angle at rest and straining. (Mibu et al. 2001) The traditional test is performed with fluoroscopy although magnetic resonance imaging, developed more recently, has the advantages of better image resolution and lack of radiation. (Kanmaniraja et al. 2021) Additionally, other pelvic floor disorders as enteroceles, bladder, and uterovaginal prolapse can be visualized when the vagina and bladder are opacified. Dynamic anorectal ultrasound is another image modality that in expert hands can be a valuable tool to evaluate the pelvic floor. (Murad-Regadas et al. 2008)

Anorectal manometry - conventional catheters that incorporate water-perfused, air-charged or solid-state sensors, as well as high-resolution manometry can be used. The rectoanal pressure pattern can indicate causes of DDs, for example decreased propulsive force, paradoxical contraction or both. (Ratuapli et al. 2013; Raza & Bielefeldt 2009). The London protocol standardized the several steps that should be performed during the manometry including resting tone, squeeze, reflex and evaluation of sensitivity. (Carrington et al. 2020)

Anal electromyography – the electric activity is recorded by electrodes mounted on an acrylic anal plug or taped to the perianal skin and it is used to identify defecation dyssynergia and also to provide biofeedback training for DD. (Bharucha & Rao 2014)

CHAPTER 2. RATIONALE

When we look at the global epidemiological data regarding constipated patients, we realize that there is a lot of data to explore. There is no information regarding the CC epidemiology in the Portuguese population. Moreover, the clarification of associated factors, toilet behaviours and patients' healthcare use can enhance clinical management.

Regarding the DD in the spectrum of CC, the previously described physiological evaluation is not always easily accessible and can be cumbersome. (Schmulson & Drossman 2017; Noelting et al. 2016) Moreover, the findings on these different tests may not be in agreement between each other's or with patients complains. (Bordeianou et al. 2011; Rao et al. 2004) For example, 30% of patients with marked defecatory symptoms have negative tests for DDs (Rao et al. 2004) and results compatible with DDs are documented in around 25% of healthy individuals. (Eltringham et al. 2008; Rao et al. 2006; Rao et al. 1999; Voderholzer et al. 1997; Jones et al. 1987) Another aspect to take into account is the cost involved in the evaluation of constipated patients. American studies report costs of healthcare utilization for CC as high as 500 dollars-patient-year while the exact impact of CC diagnostic assessment and treatment in Western Europe healthcare systems is unknown. (Dik et al. 2014) With the nowadays cost-effectiveness constraints, it may be impossible to perform the recommended physiological evaluation to all constipated patients seeking a medical consultation. And we know that DD represent a large subgroup of the constipated patients and that they have a different management approach. They should not miss proper treatment in the consequence of a DD underdiagnosis. So, a low-cost screening approach of constipated individuals that could promote an adequate selection of patients for complementary anorectal evaluation seems ideal.

Our first approach to this topic was the identification of possible low-cost tools in the anorectal evaluation followed by an extensive review of the literature to assess the value of low-cost tools in constipated patients' evaluation. (Caetano et al. 2016) The BET and the DRE were the selected low-cost tools. Our meta-analysis evaluated a total of 2329 patients and calculated a pooled sensitivity and specificity for the BET of 67% and 80% respectively and a pooled sensitivity and specificity for the DRE of 80% and 84%, as described in Table 4 and 5, respectively.

Table 4 - Summary of Studies with Balloon Expulsion Test (from Caetano et al. 2016)

<i>Study</i>	<i>N</i>	<i>BET (Simulated stool, volume (ml), body position, time (min))</i>	<i>Comparative test (used criteria)</i>	<i>Se</i>	<i>Sp</i>	<i>PPV</i>	<i>NPV</i>
<i>Kassis et al.</i>	61	<i>W 50 S 2</i>	<i>HRM and/or DEF pr-pc or pr-nr, ce-i</i>	33	80	71	45
<i>Chiarioni et al.</i>	236	<i>W 50 S 2</i>	<i>ARM pr-pc or pr-nr</i>	85	71	77	80
<i>Rao et al.</i>	100	<i>W 50 S 3</i>	<i>ARM pr-pc</i>	60	1	100	52
<i>Chiarioni et al.</i>	52	<i>W 50 S 5</i>	<i>ARM pr-pc or pr-nr</i>	94	75	89	86
<i>Ratuapli et al.</i>	295	<i>W 50 S 3</i>	<i>HRM pr-pc or pr-nr</i>	29	78	39	70
<i>Raza and Bielefeldt</i>	132	<i>A 50 S 2</i>	<i>ARM pr-pc or pr-nr</i>	76	92	92	80
<i>Minguez et al.</i>	130	<i>W SD S 1</i>	<i>ARM + DEF pr-pc or pr- nr, ce-i</i>	88	89	64	97
<i>Mibu et al.</i>	46	<i>A 20 S</i>	<i>DEF ce-i</i>	41	92	82	63
<i>Glia et al.</i>	134	<i>W 60 S</i>	<i>DEF ce-i or ce-f</i>	37	88	71	64
<i>Halligan et al.</i>	74	<i>W 10</i>	<i>DEF ce-i or ce-f</i>	87	63	51	91
<i>Jones et al.</i>	32	<i>W 50</i>	<i>EMG i</i>	75	88	95	54
<i>Rao et al.</i>	35	<i>W 50 S 5</i>	<i>ARM + DEF/CTT pr-pc or pr-nr, ce-i, stt</i>	89	76	80	87
<i>Bordeianou et al.</i>	123	<i>A 60 S 5</i>	<i>DEF ce-i</i>	52	58	57	54

Legend:

BET – balloon expulsion test, HRM – high resolution manometry, ARM – anorectal manometry, DEF – defecography, EMG – electromyography. CCT – colonic transit time

BET: W – water, A – air, SD – sustained desire to evacuate, S – seated position

HRM or ARM: pr-pc (puborectalis paradoxical contraction) or pr-nr (puborectalis non-relaxing)

DEF: ce-i (contrast evacuation impaired) or ce-f (contrast evacuation failed in 30 s)

EMG: i (activity increased)

CTT: stt (slow transit time)

Table 5 - Summary of Studies with Digital Rectal Examination (from Caetano AC et al. 2016)

<i>Study</i>	<i>N</i>	<i>DRE (used criteria)</i>	<i>Comparative test (used criteria)</i>	<i>Se</i>	<i>Sp</i>	<i>PPV</i>	<i>NPV</i>
<i>Glia et al.</i>	268	<i>2 of as-pc/as-nr, pe- i, pd-a</i>	<i>HRM (type-IV DD)</i>	93	59	91	66
<i>Tantiplachiva et al.</i>	209	<i>2 of as-pc/as-nr, am-nc, pd-a</i>	<i>ARM + BET or CTT pr-p or pr-nr, ne, stt</i>	73	85	97	31
<i>Bannister et al.</i>	168	<i>pr-pc</i>	<i>ARM + CTT</i>	83	95	98	65
<i>Halligan et al.</i>	136	<i>pr-pc</i>	<i>DEF + EMG aa-ni, i</i>	58	88	62	87

Legend:

DRE – digital rectal examination, HRM – high resolution manometry, ARM – anorectal manometry, DEF – defecography, EMG – electromyography, CCT – colonic transit time

DRE: as-pc (anal sphincter paradoxical contraction), as-nr (anal sphincter non-relaxing), am-nc (abdominal muscles not contracted) pd-a (perineal descent absent, pe-i (push effort impaired)

HRM or ARM: pr-pc (puborectalis paradoxical contraction) or pr-nr (puborectalis non-relaxing)

DEF: aa –ni (anorectal angle not increased)

EMG: i (activity increased)

CTT: stt (slow transit time)

BET: ne (not expelled a 50 ml water balloon in 1 minute)

However, we faced diverse challenges: variable diagnostic criteria, different protocols of physiological tests, lack of definitions for positive results. (Orkin et al. 2010; Tantiphlachiva et al. 2010) For example, regarding the BET, we found that the technique was not standardized in terms of time, volume, position and material used in the procedure. (Kassis et al. 2015; Chiarioni et al. 2014; Minguéz et al. 2004; Glia et al. 1998) Finally, the meta-analysis showed the importance of the BET and the DRE in the investigation of constipated patients, but did not demonstrate their capability as screening tools of DD. (Caetano et al. 2016)

Besides these potential low-cost tools, we were curious regarding clinical scores, specifically targeting the DD, that could be tailored and integrated in a screening algorithm alongside the referred low-cost tools. Two scores reporting to DD were identified - Altomare score and Renzi score. (Renzi et al. 2013; Altomare et al. 2008) The Renzi score seemed more suitable to our purposes (Table 6).

Table 6 – Renzi score for defecations disorders

Symptoms/variables	0	1	2	3	4
Excessive straining	Never	Rarely	Sometimes	Usually	Always
Incomplete rectal evacuation	Never	Rarely	Sometimes	Usually	Always
Use of enemas/laxative	Never	Rarely	Sometimes	Usually	Always
Vaginal/perineal digital pressure	Never	Rarely	Sometimes	Usually	Always
Abdominal discomfort/pain	Never	Rarely	Sometimes	Usually	Always

An evaluation of these low-cost tools, with consistent methodology, eventually incorporating a clinical score, seemed attractive in order to simplify the CC algorithmic approach.

CHAPTER 3. AIMS

Our aims were:

- * To obtain epidemiological data of CC in the local community
 - Determination of CC prevalence, and in its FC and IBS-C subtypes, in a representative sample of a European Mediterranean population, using the recent Rome IV criteria;
 - Analysis of a diversity of factors that can be associated with CC;
 - Explore toilet behaviours and potential associations with bowel habits
 - Evaluation of patients' self-management and healthcare seeking behaviour in CC, and in its FC and IBS-C spectrum.

- * To evaluate the performance of low-cost tests in the evaluation of constipated patients
 - Validation of the Portuguese version of Renzi clinical score;
 - Optimization of the BET technique output;
 - Evaluation of the BET, the DRE and de Renzi clinical score as separate or combined tests.

PART II.

RESULTS

CHAPTER 4

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Constipation: Prevalence in the Portuguese community using Rome IV—Associated factors, toilet behaviours and healthcare seeking

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Abstract

Background: Chronic constipation (CC) is a major public health condition and CC management remains challenging.

Objective: We aimed to evaluate the CC (and subtypes) prevalence in a Southern Europe Mediterranean country using Rome IV criteria, and to assess related factors, toilet and healthcare seeking behaviours.

Methods: Cross-sectional epidemiological survey, conducted in general community and representing the Portuguese population according to sex and age. The questionnaire covered bowel habits, factors potentially associated with CC (demographic, health/lifestyle, toilet behaviours) and data regarding healthcare seeking.

Results: From the study data of 1950 individuals were analyzed. The answer rate was 68% and 1335 questionnaires were available for calculation. The CC prevalence was 17.8%, with respectively 9.3% of Functional Constipation (FC) and 8.5% of Irritable Bowel Syndrome - subtype constipation (IBS-C). The likelihood of constipation was significantly higher in younger (OR 1.01; 95% confidence interval [CI], 1.007–1.031), solo (OR 2.48; 95% CI, 1.7–3.47) and low-income (OR 2.40; 95% CI, 1.77–3.47) individuals. Constipated individuals spent more time at defecation, longer than 5 min ($p = 0.001$), and had particular toilet behaviours (absence of a morning pattern [$p = 0.008$], the use of triggers [$p = 0.001$] and reading/technological material [$p = 0.006$]) to facilitate the evacuation. Only 39% of affected individuals sought medical advice, mainly IBS-C patients ($p = 0.018$).

Conclusion: Chronic constipation seems to impact 1 in each 5 Portuguese. Constipated patients are younger, solo, less active and with low income. They develop a clear toilet behaviour profile. FC and IBS-C patients assume particular behaviours.

KEYWORDS

chronic constipation, healthcare, prevalence, Rome IV, toilet behaviours

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INTRODUCTION

Chronic constipation (CC) is a symptom-based disorder that includes a broad set of complaints as decreased stool frequency, straining, incomplete evacuation and sense of anorectal blockage for more than 3 months. CC is either a secondary condition (due to other disease, medications or anatomic alterations) or, more frequently, a primary disorder without an evident underlying cause (related to neuromuscular or sensory-motor dysfunction).¹ This is one of the most frequent gastrointestinal diagnoses made in ambulatory medicine clinics, in addition, economic cost and adverse implications on the quality of life make CC a major public health issue.¹⁻³

The worldwide prevalence of CC among adults is estimated to be around 15%.¹ However, when looking at three large systematic reviews including studies of community samples, we realize that the prevalence varies widely.⁴⁻⁶ This wide variation may be in part due to differences in populations as age groups, culture, diet and environment.⁷ For instance, in Southern Europe or Mediterranean countries, Soares et al.⁵ describes a CC prevalence between 5% and 20%. Nevertheless, in the last 20 years there is only 1 study with more than 1000 participants, reporting the CC epidemiology in the general population, from France.⁸

Another important aspect that may contribute to the prevalence variation is the difference in the definition of constipation in each study.⁷ Many of these community surveys used either self-report constipation or questionnaires based on one or some of the symptoms described in previous iterations of the Rome criteria.^{5,7}

The Rome criteria were developed for use as a standard definition of primary CC, its most recent edition – the Rome IV criteria – categorize patients as having functional constipation (FC), constipation-predominant irritable bowel syndrome (IBS-C) or defecatory disorders (DDs)^{9,10} as described in Table 1,^{11,12} but to our knowledge, it has not yet been properly applicable in adult national prevalence studies.

Associated factors such as gender, age, dietary habits, physical inactivity, socioeconomic level, psychological parameters and vaginal delivery were frequently implicated in the development of CC according to available literature.^{1,13,14} Regarding dietary habits, there are data suggesting that the Mediterranean diet (MD) might be beneficial in ameliorating functional gastrointestinal symptoms in children and adolescents, through the increased fibre and antioxidant consumption and the low intake of saturated fats and oligosaccharides¹⁵ but there is no information regarding adult population.

An additional interesting feature is that only a minority of patients, approximately 25% of those affected, seek specific medical advice, making the information regarding self-management and healthcare use scarce and not well understood.^{16,17}

Thus, CC is an economic burden and is important to know its accurate prevalence in populations, moreover, the clarification of associated factors and patients' behaviours can be very important in enhancing clinical management.

Key summary

1. Summarise the established knowledge on this subject

- The worldwide prevalence of Chronic constipation (CC) varies significantly.
- High economic cost and low quality of life make CC a major public issue.
- Data regarding associated factors and patients' behaviours can enhance clinical management.

2. What are the significant and/or new findings of this study?

- CC seems to impact 1 in each 5 European Mediterranean individuals.
- Constipated patients are younger, solo, less active and with low income.
- Constipated individuals develop a clear toilet behaviour profile.

AIM

The aim of this study is to determine the prevalence of CC in a representative sample of a European Mediterranean population, using the recent Rome IV criteria. As secondary aims, we intend to analyse the association of a diversity of factors with CC, and to evaluate the patient self-management and his healthcare seeking behaviour in CC, and in its FC and IBS-C subtypes.

METHODS

Study design and population

This was a cross-sectional study with an epidemiological survey, conducted in the general community. It was carried out in the municipality of Braga located in the North Coast of Portugal, a Mediterranean country of Southern Europe. A total of 178,558 individuals constituted the eligible population older than 18 years (single inclusion criterion). For an expected prevalence of CC of 20%, an accuracy of 4% and a 95% confidence interval (CI), we calculated a sample size per strata. Using the central data of the region population, a systematic, stratified by age, random sampling was arbitrarily performed, considering three groups: 18-39, 40-64 and > 64 years. With an expected response of 60%, the global sample required totalled 1920 subjects. Using the local health authority registries from the resident population of Braga, our primary sample population was randomly selected after applying the criteria required to obtain a cohort that represents the adult Portuguese population. Inquiries were sent to each 13 Health Care Centres of urban and rural areas of the municipality of Braga. The General Practitioner excluded in advance potential responders who had a known medical history

TABLE 1 Rome IV criteria of chronic constipation subtypes

Diagnostic criteria (a) for functional constipation
1. Must include 2 or more of the following:
a. Straining during more than one-fourth (25%) of defecations
b. Lumpy or hard stools (BSFS 1–2) more than one-fourth (25%) of defecations
c. Sensation of incomplete evacuation more than one-fourth (25%) of defecations
d. Sensation of anorectal obstruction more than one-fourth (25%) of defecations
e. Manual manoeuvres to facilitate more than one fourth (25%) of defecations
f. Fewer than 3 spontaneous bowel movements per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome
Diagnostic criteria (a) for irritable bowel syndrome with constipation
1. Recurrent abdominal pain at least 1 day a week with 2 or more of the following:
a. Related to defecation
b. Related to change in frequency of stools
c. Related to change in form of stools
2. Lumpy or hard stools (BSFS 1–2) more than one-fourth (25%) of defecations
Diagnostic criteria (a) for functional defecation disorders
1. The patient must satisfy diagnostic criteria for functional constipation and/or irritable bowel syndrome with constipation
2. During repeated attempts to defecate, there must be features of impaired evacuation, as demonstrated by 2 of the following 3 tests:
a. Abnormal balloon expulsion test
b. Abnormal anorectal evacuation pattern with manometry or anal surface EMG
c. Impaired rectal evacuation by imaging

Note: (a) Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Abbreviations: BSFS, bristol stool form scale; EMG, electromiography.

involving or influencing bowel functioning (bowel surgery, inflammatory bowel diseases, endocrine and neurological disorders, and medications like opioids and antipsychotics) considered exclusion criteria. The participants were invited to fulfil the written or the online form of the questionnaire, between September 2020 and May 2021.

Questionnaire

A questionnaire with 25-items divided in several sections was developed. The first section included demographic information as age and gender. Social class was evaluated according to professional

occupation and activity, income (dichotomized in high and low income using the cut-off of 1000 euros per month) and level of completed education. Marital status was dichotomized in solo (single, divorced and widow) and couple (marriage and common-law marriage).

The second section included medical and lifestyle data. Medical history (dichotomized into healthy when no disorders was described and disease status when one or more disorders were described) surgical history and medication use was collected as well. Physical activity, smoking habits and diet were also evaluated. Diet was assessed by means of a validated food frequency questionnaire regarding MD.¹⁸ Adherence to the traditional MD was assessed by a 10-point scale, as described by Trichopoulou et al.¹⁸ - range of score from 0 (minimal adherence) to 9 (maximal adherence). The cut-off of six points was defined to differentiate MD adherents and MD non-adherents, as proposed previously by several authors for this purpose.^{18–20}

The third section included data regarding bowel habits that allowed us to define the study population in terms of regular bowel function (control group) and FC or IBS-C (constipated group). The diagnostic criteria used to define the constipated group were the consensus criteria of Rome IV as detailed in Table 1. Some patients satisfied criteria for FC and IBS-C, in this case according to the Rome criteria specifications, the patients who had symptoms of IBS-C and FC were classified as IBS-C.

Questions regarding self-management and healthcare seeking were included in the last section of the questionnaire - descriptive healthcare seeking, the use of over-the-counter and/or prescribed laxatives and other complementary techniques, proctological conditions, as well as some toilet behaviours (evacuation pattern, squatting device, triggers as coffee or cigarette, the use of reading or technological material in the toilet).

A pilot study was conducted with this questionnaire, administering it to 10 subjects from a socio-cultural setting similar to that of the study population. The questionnaire was found to be easy to understand and answer.

Ethical considerations

The study project was approved by the Ethic Commissions of Braga Hospital and School of Medicine of Minho University and by the North Region Health Administration. Informed consent was obtained from all participants, and Portuguese regulations applicable to the management of personal data was followed at all times.

Data analysis

Descriptive statistics for continuous variables were reported as median (interquartile range, IQR) while for categorical variables were reported as frequency (%). The Pearson chi square test was used to compare categorical variables and the Wilcoxon test to compare

continuous data. A Multiple Linear Regression Model was performed for each of the significant variables previously calculated when considered adequate. All statistical tests were two-sided and a probability level of 0.05 was used to indicate statistical significance. All the statistical analyses were conducted using the software SPSS 27.0 (IBM).

RESULTS

A total of 1950 questionnaires were delivered, and overall, 1382 subjects replied. Despite the initial exclusion criteria, additional 47 responders were excluded due to colorectal disease or surgical history ($N = 10$), chronic use of opioids ($N = 4$) and lack of more than 50% of the information ($N = 33$), making 1335 questionnaires available for analysis (68%).

General demographic data

Regarding the study population and following the items order of subsequent analysis in Table 3: 895 (67%) were female with median age of 45 (IQ 19) years; 34.2% with low qualified professions, 12.1% professionally not active and 21.9% with low income; the level of education was low (up to ninth grade/middle school) in 17.7%, median (up to 12th grade/high school) in 31.1% and superior in 51.3% of participants; 68% lived as a couple.

There was a slightly higher proportion of female responders compared with global population (66% vs. 54%) but there were no other statistically significant differences in the baseline characteristics of individuals in the study population and in the Portuguese population.²¹

Prevalence of CC and subgroups (FC and IBS-C)

The prevalence of CC (FC plus IBS-C) in the study sample was 17.8% ($N = 237$). Ninety-nine patients satisfy criteria for FC and IBS-C, but according to the Rome criteria 113 patients were classified as IBS-C and 124 as FC. The subgroup prevalence was 9.3% for FC and 8.5% for IBS-C.

Regarding the items of Rome IV criteria that establish the diagnosis of constipation (displayed in Table 2), as expected they were all also more frequent in both subgroups of individuals. Besides the known criteria another item stood up: time at defecation >5 min. Time at defecation >5 min was more frequent in constipated individuals (56.4% vs. 31.9% $p = 0.001$) and that was also true for both FC (59.5% vs. 30.8% $p = 0.001$) and IBS-C (55.9% vs. 39.2% $p = 0.002$) subgroups.

Another unexpected data was the reported use of laxative (although unfrequently) by 20 individuals with no bowel complains.

CC related factors and behaviours

Table 3 describes the main characteristics of the constipated group and the control group.

1. CC related factors (demography and health/lifestyle):

Demography - Constipated individuals were younger (49 vs. 51 years old, $p = 0.014$), professionally not active (32.2% vs. 35.1% $p = 0.001$), single (49.6% vs. 28.5% $p = 0.001$) and with low-income (37.9% vs. 18.3% $p = 0.001$) in comparison to the control group.

Lifestyle - Constipated individuals reported more frequently comorbidities (91.2% vs. 66.7% $p = 0.001$), and less practice of physical activity (51.5% vs. 60.7% $p = 0.049$). There were no differences regarding other items, including MD score and MD adherence.

On evaluation of these CC factors, the univariate analyses revealed that age, professional activity, marital status and income had a significant influence on the likelihood of constipation, but professional activity was not sustained in the multivariate analysis subsequently performed (Table 4). There were no significant interactions between the remaining variables used. The likelihood of constipation was significantly higher in younger population (OR 1.0019; 95% CI, 1.007–1.031). The solo and low-income responders were also more likely to suffer from constipation (OR 2.48; 95% CI, 1.77–3.47 and OR 2.40; 95% CI, 1.7–3.38 respectively).

2. Toilet behaviours

The less frequent morning evacuation habit (66.1% vs. 79.2% $p = 0.008$), the use of triggers to facilitate evacuation (51.7% vs. 15.3% $p = 0.001$) and the use of reading or technological material in the toilet (64.7% vs. 52.3% $p = 0.006$) were more frequent in the constipated group.

3. Healthcare seeking

Constipated patients were more concerned about their bowel habits (67.1% vs. 28.9% $p = 0.001$) and sought more frequently any form of healthcare advice (61.1% vs. 29.7% $p = 0.001$) - specified in absolute numbers as medical (93 vs. 64), pharmaceutical (69 vs. 34), alternative (24 vs. 12) and psychological (3 vs. 2) advice. Constipated patients use more laxatives (27% vs. 6.5% $p = 0.001$) and suffer more frequently from proctological conditions as haemorrhoidal disease (61.2% vs. 39.5% $p = 0.001$) and anal fissure (23.5% vs. 15.4% $p = 0.03$). When calculating specifically the medical seeking behaviour of this CC population we find the rate of 39%.

FC and IBS-C subgroup evaluation

Comparing FC and IBS-C patients, no differences were found in demographic or health/lifestyle characteristics. Considering the toilet and healthcare seeking behaviours, some differences were raised (Table 5). Only FC patients reported an evacuation (absence of) regularity, and the use of triggers and squatting devices for evacuation. IBS-C patients were more concerned about their bowel habits

TABLE 2 Individualized Rome IV criteria in constipated patients and controls

	FC + IBS-C (n = 237)	Control (n = 1098)	P value
1. CC related factors			
Demography			
Female	167 (70.5%)	728 (66.3%)	0.216
Age (median years/interquartile range)	49/28	51/26	0.014
Low qualification profession	58 (32.2%)	319 (35.1%)	0.195
Professionally not active	47 (19.8%)	115 (10.5%)	0.001
Low income	81 (37.9%)	173 (18.3%)	0.001
Scholarity			
9th grade	37 (15.9%)	193 (18%)	0.735
12th grade	75 (32.3%)	330 (30.8%)	
Superior	120 (51.7%)	548 (51.2%)	
Marital status			
Couple (married and common law)	115 (50.4%)	767 (71.5%)	0.001
Single (single, divorced, widow)	113 (49.6%)	307 (28.5%)	
Lifestyle			
Healthy status	136 (66.7%)	964 (91.2%)	
BMI	24.5/4.4	24/4.5	0.702
Water intake (<1.5 L)	170 (85.4%)	227 (82.2%)	0.356
MD adherence (>5 points)	137 (67.8%)	192 (69.6%)	0.684
Physical activity	102 (51.5%)	167 (60.7%)	0.049
Smoking habits	89 (44.7%)	109 (39.6%)	0.268
2. Toilet behaviours			
Morning evacuation	72 (66.1%)	210 (79.2%)	0.008
At home evacuation	208 (98.6%)	267 (96.4%)	0.137
Squatting devices	9 (8.4%)	9 (3.6%)	0.068
Triggers	61 (51.7%)	163 (15.3%)	0.001
Digital or printed material toilet use	139 (64.7%)	149 (52.3%)	0.006
3. Healthcare seeking			
Concerns regarding bowel habits	139 (67.1%)	80 (28.9%)	0.001
Seek healthcare for bowel habits	124 (61.1%)	80 (29.7%)	0.001
Haemorrhoidal disease	123 (61.2%)	109 (39.5%)	0.001
Anal fissure	46 (23.5%)	41 (15.4%)	0.03

Abbreviation: BMI, Body mass index.

(74.7% vs. 60.7% $p = 0.032$) and sought more frequently any form of healthcare advice (69.9% vs. 53.6% $p = 0.018$).

DISCUSSION

Our population presented a constipation rate of 17.8%, in accordance with other European demographic studies with prevalence between 19.8 and 20.2 per 100 inhabitants.⁶ When considering

small and large available Mediterranean studies of the last 2 decades, we are close to the French (22.4%),⁸ the Spanish (19.2%)²² and in a less extent the Greek results (15%).²³ Most of these studies used self-reported information, which have identified bias limitations, but some applied simultaneously the previous Rome criteria.^{7,22,23} It is remarkable that the prevalence of CC seems to remain consistent using the Rome IV criteria. Aside the criteria discussion, the similarity of constipation rates in the developed countries may partially be due to the similar lifestyle, physical

TABLE 3 Main characteristics of the constipated group and the control group

	FC + IBS-C (n = 237)	Control (n = 1098)	P value
Less than 3 defecations per week	49 (21%)	3 (1%)	0.001
Use of laxatives	63 (27%)	20 (6.5%)	0.001
Time at defecation >5 min	132 (56%, 4%)	96 (31.9%)	0.001
Hard stools	212 (91%)	107 (38.9%)	0.001
Straining	187 (82.4%)	3 (1.3%)	0.001
Sensation of incomplete evacuation	178 (77.7%)	38 (15.8%)	0.001
Manual manoeuvres to evacuate	48 (28.1%)	2 (1%)	0.001
Abdominal pain related to defecation	114 (56.7%)	29 (13.1%)	0.001
Abdominal pain related to change in frequency of stools	107 (51%)	29 (12.7%)	0.001
Abdominal pain related to change in form of stools	133 (63.9%)	50 (21.9%)	0.001

TABLE 4 Prevalence and likelihood of constipation

	Prevalence (%)	P value	Likelihood of constipation Multivariate logistic regression		
			OR	95% CI	P value
Age (median years)	49	0.014	1.019	1.007–1.031	0.001
Low income	37.9%	0.001	2.40	1.7–3.38	0.001
Marital status					
Solo (single, divorced, widow)	49.6%	0.001	2.48	1.77–3.47	0.001

TABLE 5 Comparison of toilet behaviours and healthcare seeking in Functional Constipation (FC) and IBS-C individuals

	FC (n = 124)	IBS-C (n = 113)	P value	Missing data (%)
Toilet behaviours				
Morning evacuation	72 (66.1%)	97 (98%)	0.001	12%
At home evacuation	100 (100%)	108 (97.3%)	0.098	11%
Squatting devices	9 (8.4%)	2 (2%)	0.001	14%
Triggers	61 (51.7%)	21 (20%)	0.001	7%
Digital or printed material toilet use	73 (63.5%)	66 (66%)	0.7	9%
Healthcare seeking				
Concerns regarding bowel habits	68 (60.7%)	71 (74.7%)	0.032	13%
Seek healthcare for bowel habits	59 (53.6%)	65 (69.9%)	0.018	14%
Haemorrhoidal disease	68 (63%)	55 (59.1%)	0.579	15%
Anal fissure	24 (23.3%)	22 (237%)	0.953	17%

activity and socioeconomic level as well as common dietary habits of these populations. In fact, we hypothesized that MD could influence the prevalence rate in our Mediterranean population, but it was not confirmed as discussed below.

With the Rome IV criteria, we could discriminate the population prevalence of the two main subtypes of CC (FC - 9.3% and IBS-C - 8.5%) and this division also allowed us to evaluate the association of certain specific features. The Rome Foundation recently published their Global Study results and calculated a worldwide

prevalence of FC and IBS-C of 11.7% and 1.3% respectively in a combined Internet and household survey in 26 countries.²⁴ The most important limitation of their study was the lack of national representation, thus, our is the first European population survey using the Rome IV criteria to define constipation in an adult epidemiologic study. In the spectrum of the primary CC we were not able to categorize and calculate the prevalence for DD, which is around 50% in the constipated population according to other studies^{1,11} and our own experience.¹²

A secondary aim was to identify factors related to CC. Female gender was not significantly associated with CC as described by other authors.⁵⁻⁸ A reasonable explanation is the female preponderance of the survey responders, including the control group, a bigger study population would probably reveal that association. Constipated patients were slightly younger than controls as described by some authors but not by others.²²⁻²⁴ Verkuil S et al. brilliantly explore these apparently contradictory conclusions by reporting different clinical patterns of constipation symptoms in different age groups and pointing several pathophysiological differences as the reason.²⁵ In our population, being solo and professionally not active were associated with constipation. This might be explained by less regularity of routines in these conditions. Individuals of lower social, economic and educational level have a tendency towards higher constipation rates according to Bytzer et al.¹⁴ and Peppas et al.⁶ but in our sample, only low-income was associated with constipation. Possibly educational, social and economic level are not so closely related in the Portuguese population as in other populations, explaining why we identify the association with low-income but not with educational or professional qualification. Although out of the scope of this manuscript, among these low-income responders, we found an associated behaviour pattern of lack of exercise, no smoking and poor adherence to MD. Constipated individuals report less frequently a healthy condition compared to controls in agreement with other studies, that state the well-known association with comorbidities as cardiovascular, digestive or psychological conditions.^{6,26} Surprisingly there were no differences in terms of diet factors such as number of meals, water intake, food restrictions and adherence to a MD. MD was extensively studied in terms of cardiovascular benefit and overall survival, but regarding bowel habits, as far as we know only Agakidis et al.¹⁵ concluded that good adherence to the MD in a younger population was associated to lower prevalence of functional gastrointestinal diseases.¹⁵ Maybe a bigger sample could uncover some of these associations. However, poor diet habits are associated with low income²⁷ an important demographic factor identified in our CC population. Or else, perhaps our participants may not be keen at recalling the variation of their lifestyle behaviours. Physical inactivity was more frequent in constipated individuals as described by others.²⁸ In our opinion our data adds evidence pointing to the continuous effort in terms of patient education regarding exercise.

We confirm that all items of Rome IV criteria were associated with the diagnosis of FC and IBS-C showing that they are all strong and associated criteria. The time at defecation >5 min was more frequent in constipated individuals and in both subgroups. Could be this feature additionally important when we evaluate bowel habits?²⁹ In a study with 102 patients, Garg and Singh associate the 'TONE' mnemonic habits (T, 3 min at defecation; O, once-a-day defecation frequency; N, no straining during passing motions; E, enough fibre) with improvement in deranged defecation habits and haemorrhoidal disease.²⁹ Verkuil S et al. also identify straining of more than 5 min as well as daily failure to defecate as reliable indicators of CC²⁵ We think that time at defecation is probably underestimated and that it is

important to integrate this item in our clinical interview and to work it in our therapeutic plan with constipated patients.

Toilet behaviours associated with CC were the reduced morning evacuation habit, the use of reading or technological material, and the use of triggers (such as coffee, cigarette, gym) to help evacuation. The absence of the morning evacuation habit is probably explained by the pathophysiological mechanisms of constipation, making harder to control the time-scheduled bowel evacuation. Reading and technological material use, is described by more than 60% of the constipated subjects and that also is an echo of our times. As Goldstein et al. conclude in their study and we also infer from our survey, the use of reading or technological material seems to relax individuals but not help specifically the evacuation (at least not consciously).³⁰ When looking at subtype analysis, FC patients do not present an evacuation regularity, and this can explain the need for the more frequent use of triggers and squatting devices – the absence of an evacuation pattern pressures these patients for a rigid toilet commitment to improve the bowel habits in FC, not so demanding with the more intermittent nature of IBS complains.

Our study also examined the use of healthcare resources by constipated individuals. The seek for medical, pharmaceutical, alternative and psychological help was associated with constipation as well as the use of (over-the-counter and prescribed) laxatives. Similar to Galvez et al. that reported seeking of healthcare in over 40% of constipated subjects in their study population, we identify in our constipated individuals 39% of specific medical seeking and 67% of seeking for any form of help regarding their bowel habits.¹⁶ Maybe the proximity to the pharmacist, herbalist or shopkeeper and ease of access to laxatives (even the controls described its occasional use) can explain the growing seek of any form of help regarding bowel habits. At this point, there was also a significant difference between our subgroups - the concern and healthcare for bowel habits are reported more frequently by IBS-C individuals compared to FC patients. This can be explained by the abdominal pain that characterizes IBS, a troublesome symptom that probably raises fears in these commonly anxious patients.³¹

Advantages of this study are its large size and its reliance on a sample of the general population. The systematic sampling and age stratification to define our study population reduced selection bias. Most epidemiological studies comprise sample selection based on recruitment of volunteers, occupational groups, commercial databases or student populations or are based on doctor-delivered questionnaires or hospital diagnoses upon admission and it increases the risk of information bias.¹⁶ The main weakness of the study is the sample size that could be even larger and the use of recall information; by other hand, additional information could have been collected, for instance gynaecological background in this predominant female population.

As pointed out, this is the first epidemiological study regarding CC in an adult population of a European Mediterranean country using extended Rome IV Criteria. As far as we know, it is also the first time that an exhausting evaluation of associated factors, toilet

behaviours and healthcare seeking is achieved, helping us to understand better constipated individuals.

CONCLUSION

Using Rome IV criteria, the prevalence of CC is 17.8% (FC - 9.3% and IBS-C - 8.5%) in this European survey. This condition was associated with younger age, being solo, professionally not active, having a low-income, and a reported unhealthy condition and less practice of exercise. Constipated individuals spent more time at defecation and have specific toilet behaviours (as the absence of morning pattern, the use of triggers, the use of laxatives and the use of reading/technological material). Although they seek for a diversity of healthcare support, only 39% of affected individuals seek for medical advice. The toilet behaviours seem more complex in FC, inversely the healthcare seeking behaviour looks more frequent in IBS-C.

AUTHOR CONTRIBUTIONS

Ana Célia Caetano contributed for the conception and draft of this article; Dalila Costa contributed for the statistical analysis, Silva-Mendes Sofia contributed with data collection, Jorge Correia-Pinto and Carla Rolanda contributed for the critical revision and submission of this articles. There is no conflict of interest or disclosure to formulate. Study materials will be made available to other researchers upon request.

CONFLICT OF INTEREST

We declare there is no conflict of interest or disclosure to formulate.

DATA AVAILABILITY STATEMENT

Deidentified individual participant data and the study protocol can be included as a data supplement available with the online version of this article.

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REFERENCES

- Bharucha AE, Lacy B. Mechanisms, evaluation, and management of chronic constipation. *Gastroenterology*. 2020;158(5):1232–49.e3.
- Bharucha AE, Wald A. Chronic constipation. *Mayo Clin Proc*. 2019;94(11):2340–57. <https://doi.org/10.1016/j.mayocp.2019.01.031>
- Dik VK, Siersema PD, Joseph A, Hodgkins P, Smeets HM, van Oijen MG. Constipation-related direct medical costs in 16 887 patients newly diagnosed with chronic constipation. *Eur J Gastroenterol Hepatol*. 2014;26(11):1260–6. <https://doi.org/10.1097/meg.000000000000167>
- Mugie SM, Benninga MA, Di Lorenzo C. Epidemiology of constipation in children and adults: a systematic review. *Best Pract Res Clin Gastroenterol*. 2011;25(1):3–18. <https://doi.org/10.1016/j.bpg.2010.12.010>
- Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. *Am J Gastroenterol*. 2011;106(9):1582–91. <https://doi.org/10.1038/ajg.2011.164>
- Peppas G, Alexiou VG, Mourtzoukou E, Falagas ME. Epidemiology of constipation in Europe and Oceania: a systematic review. *BMC Gastroenterol*. 2008;128(1):5. <https://doi.org/10.1186/1471-230x-8-5>
- Werth B, Williams K, Fisher M, Pont LG. Defining constipation to estimate its prevalence in the community: results from a national survey. *BMC Gastroenterol*. 2019;19(1):75. <https://doi.org/10.1186/s12876-019-0994-0>
- Siproudhis L, Pigot F, Godeberge P, Damon H, Soudan D, Bigard MA. Defecation disorders: a French population survey. *Dis Colon Rectum*. 2006;49(2):219–27. <https://doi.org/10.1007/s10350-005-0249-8>
- Schmulson MJ, Drossman DA. What is new in Rome IV. *J Neurogastroenterol Motil*. 2017;3023(2):151–63. <https://doi.org/10.5056/jnm16214>
- Simren M, Palsson OS, Whitehead WE. Update on Rome IV criteria for colorectal disorders: implications for clinical practice. *Curr Gastroenterol Rep*. 2017;19(4):15. <https://doi.org/10.1007/s11894-017-0554-0>
- Vidlock EJ, Lembo A, Cremonini F. Diagnostic testing for dyssynergic defecation in chronic constipation: meta-analysis. *Neuro Gastroenterol Motil*. 2013;25(6):509–20. <https://doi.org/10.1111/nmo.12096>
- Caetano AC, Santa-Cruz A, Rolanda C. Digital rectal examination and balloon expulsion test in the study of defecatory disorders: are they suitable as screening or excluding tests? *Can J Gastroenterol Hepatol*. 2016;8654314. <https://doi.org/10.1155/2016/8654314>
- Higgins PD, Johanson JF. Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol*. 2004;99(4):750–9. <https://doi.org/10.1111/j.1572-0241.2004.04114.x>
- Bytzer P, Howell S, Leemon M, Young LJ, Jones MP, Talley NJ. Low socioeconomic class is a risk factor for upper and lower gastrointestinal symptoms: a population-based study in 15 000 Australian adults. *Gut*. 2001;49(1):66–72. <https://doi.org/10.1136/gut.49.1.66>
- Agakidis C, Kotzakioulafi E, Petridis D, Apostolidou K, Karagiozoglou-Lampoudi T. Mediterranean diet adherence is associated with lower prevalence of functional gastrointestinal disorders in children and adolescents. *Nutrients*. 2019;11(6):1283. <https://doi.org/10.3390/nu11061283>
- Gálvez C, Garrigues V, Ortiz V, Ponce M, Nos P, Ponce J. Healthcare seeking for constipation: a population-based survey in the Mediterranean area of Spain. *Aliment Pharmacol Ther*. 2006;24(2):421–8. <https://doi.org/10.1111/j.1365-2036.2006.02981.x>
- Jones R, Ballard K. Healthcare seeking in gastro-oesophageal reflux disease: a qualitative study. *Eur J Gastroenterol Hepatol*. 2008;20(4):269–75. <https://doi.org/10.1097/meg.0b013e3282f2a5bd>
- Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348:2599–608. <https://doi.org/10.1056/nejmoa025039>
- Beunza JJ, Toledo E, Hu FB, Bes-Rastrollo M, Serrano-Martinez M, Sanchez-Villegas A, et al. Adherence to the Mediterranean diet, long-term weight change, and incident overweight or obesity: the Seguimiento Universidad de Navarra (SUN) cohort. *Am J Clin Nutr*. 2010;92(6):1484–93. <https://doi.org/10.3945/ajcn.2010.29764>
- Misirli G, Benetou V, Lagiou P, Bamia C, Trichopoulos D, Trichopoulou A. Relation of the traditional Mediterranean diet to cerebrovascular disease in a Mediterranean population. *Am J Epidemiol*. 2012;176(12):1185–92. <https://doi.org/10.1093/aje/kws205>
- <https://www.pordata.pt/Home>

22. Garrigues V, Gálvez C, Ortiz V, Ponce M, Nos P, Ponce J. Prevalence of constipation: agreement among several criteria and evaluation of the diagnostic accuracy of qualifying symptoms and self-reported definition in a population-based survey in Spain. *Am J Epidemiol.* 2004;159(5):520–6. <https://doi.org/10.1093/aje/kwh072>
23. Papatheodoridis GV, Vlachogiannakos J, Karaitianos I, Karamanolis DG. A Greek survey of community prevalence and characteristics of constipation. *Eur J Gastroenterol Hepatol.* 2010;22(3):354–60. <https://doi.org/10.1097/meg.0b013e32832bdfdf0>
24. Sperber A, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome foundation global study. *Gastroenterology.* 2021;160(1):99–114. <https://doi.org/10.1053/j.gastro.2020.04.014>
25. Verkuil S, Meinds RJ, Trzpis M, Broens PMA. The influence of demographic characteristics on constipation symptoms: a detailed overview. *BMC Gastroenterol.* 2020;20(1):168. <https://doi.org/10.1186/s12876-020-01306-y>
26. Haug TT, Mykletun A, Dahl AA. Are anxiety and depression related to gastrointestinal symptoms in the general population? *Scand J Gastroenterol.* 2002;37(3):294–8. <https://doi.org/10.1080/003655202317284192>
27. Darmon N, Drewnowski A. Contribution of food prices and diet cost to socioeconomic disparities in diet quality and health: a systematic review and analysis. *Nutr Rev.* 2015;73(10):643–60. <https://doi.org/10.1093/nutrit/nuv027>
28. Tantawy SA, Kamel DM, Abdelbasset WK, Elgohary H. Effects of a proposed physical activity and diet control to manage constipation in middle-aged obese women. *Diabetes Metab Syndr Obes.* 2017;10:513–19. <https://doi.org/10.2147/dmsos.s140250>
29. Garg P, Singh P. Adequate dietary fiber supplement and TONE can help avoid surgery in most patients with advanced hemorrhoids. *Minerva Gastroenterol Dietol.* 2017;63(2):92–6. <https://doi.org/10.23736/s1121-421x.17.02364-9>
30. Goldstein O, Shaham Y, Naftali T, Konikoff F, Lavy A, Shaoul R. Toilet reading habits in Israeli adults. *Neuro Gastroenterol Motil.* 2009; 21(3):291–5. <https://doi.org/10.1111/j.1365-2982.2008.01204.x>
31. Hu Z, Li M, Yao L, Wang Y, Wang E, Yuan J, et al. The level and prevalence of depression and anxiety among patients with different subtypes of irritable bowel syndrome: a network meta-analysis. *BMC Gastroenterol.* 2021;21(1):23. <https://doi.org/10.1186/s12876-020-01593-5>

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CHAPTER 5

Caetano AC, Dias S, Santa-Cruz A, Rolanda C. *Renzi score for obstructed defecation syndrome – validation of the Portuguese version according to the COSMIN checklist.* Arq Gastroenterol. 2018 Jan-Mar;55(1):55-60.

Renzi score for obstructed defecation syndrome – validation of the Portuguese version according to the COSMIN checklist

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ABSTRACT – Background – Recently, the Obstructed Defecation Syndrome score (ODS score) was developed and validated by Renzi to assess clinical staging and to allow evaluation and comparison of the efficacy of treatment of this disorder. **Objective** – Our goal is to validate the Portuguese version of Renzi ODS score, according to the Consensus based Standards for the selection of the Health Measurement Instruments (COSMIN) checklist. **Methods** – Following guidelines for cross-cultural validity, Renzi ODS score was translated into the Portuguese language. Then, a group of patients and healthy controls were invited to fill in the Renzi ODS score at baseline, after 2 weeks and 3 months, respectively. We assessed internal consistency, reliability and measurement error, content and construct validity, responsiveness and interpretability. **Results** – A total of 113 individuals (77 patients; 36 healthy controls) completed the questionnaire. Seventy and 30 patients repeated the Renzi ODS score after 2 weeks and 3 months respectively. Factor analysis confirmed the unidimensionality of the scale. Cronbach's α coefficient of 0.77 supported item's homogeneity. Weighted quadratic kappa of 0.89 established test-retest reliability. The smallest detectable change at the individual level was 2.66 and at the group level was 0.30. Renzi ODS score and the total (-0.32) and physical (-0.43) SF-36 scores correlated negatively. Patient and control's groups significantly differed (11 points). The change score of Renzi ODS score between baseline and 3 months correlated negatively with the clinical evolution (-0.86). ROC analysis showed minimal important change of 2.00 with AUC 0.97. Neither floor nor ceiling effects were observed. **Conclusion** – This work validated the Portuguese version of Renzi ODS score. We can now use this reliable, responsive, and interpretable (at the group level) tool to evaluate Portuguese ODS patients.

HEADINGS – Constipation, classification. Defecation. Psychometrics. Surveys and questionnaires.

INTRODUCTION

Chronic constipation is one of the five most common gastrointestinal disorders. It consumes substantial health care resources due to the high prevalence and specificity of the diagnostic tests and treatments involved. It also has a considerable impact on patients' quality of life and mental state⁽¹⁾.

Patients with functional constipation (FC) according to the Rome IV criteria, fall into one of three categories: normal transit constipation, slow transit constipation and obstructed defecation syndrome (ODS)^(2,3). The ODS is the most frequent form of FC and it can be purely functional (anismus), mechanical (retoccele, rectal prolapse) or both⁽⁴⁾.

To diagnose ODS, clinical criteria must be complemented with at least two alterations related to impaired evacuation in anorectal tests – balloon expulsion test (BET), anorectal manometry (ARM), imaging or electromyography (EMG)⁽⁵⁻⁷⁾. Therefore ODS diagnosis involves great complexity and important direct and indirect costs. A clinical score is a useful tool to categorize the severity of symptoms and evaluate post-treatment results^(8,9). Besides, it can be studied as first line evaluation instrument before step up to a more complex diagnostic approach. In 1996, Agachan et al. published the first constipation scoring system useful for the evaluation and management of constipated patients⁽¹⁰⁾. Altomare score and Renzi score are the only two published and validated tools to evaluate ODS patients.

Altomare score includes “time spent at the toilet” and “stool consistency”, items with a strong cultural influence and diet effect in our opinion. On the other hand, Renzi score is a simple questionnaire (FIGURE 1) that discriminates between healthy controls and ODS patients with sensitivity of 92% and specificity of 96%⁽⁹⁾.

Symptoms / variables	0	1	2	3	4
Excessive straining	Never	Rarely	Sometimes	Usually	Always
Incomplete rectal evacuation	Never	Rarely	Sometimes	Usually	Always
Use of enemas / laxative	Never	Rarely	Sometimes	Usually	Always
Vaginal/perineal digital pressure	Never	Rarely	Sometimes	Usually	Always
Abdominal discomfort / pain	Never	Rarely	Sometimes	Usually	Always

Sintomas / variáveis	0	1	2	3	4
Esforço excessivo	Nunca	Raramente	Às vezes	Frequentemente	Sempre
Esvaziamento rectal incompleto	Nunca	Raramente	Às vezes	Frequentemente	Sempre
Uso de clisters / laxantes	Nunca	Raramente	Às vezes	Frequentemente	Sempre
Pressão digital vaginal / perineal	Nunca	Raramente	Às vezes	Frequentemente	Sempre
Desconforto / dor abdominal	Nunca	Raramente	Às vezes	Frequentemente	Sempre

FIGURE 1. Renzi ODS score (English and Portuguese version).

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Recently, a Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist was developed in an international Delphi study to evaluate the methodological quality of studies on measurement properties of health-related patient reported outcomes⁽¹¹⁾.

To be applied in Portuguese-speaking countries, there must be a validated Portuguese version of the Renzi ODS score, what did not exist to date. Our goal is to validate the Renzi ODS score, in the Portuguese language according to the COSMIN checklist.

METHODS

Translations and cross cultural validity

After receiving authorization from the developers of the original ODS score, Renzi ODS score was translated forward (into Portuguese) by two bilingual translators. Then, two Gastroenterology's experts synthesized the results of the translation into a unique score that suffered a backward translation (into English) by two bilingual translators⁽¹²⁾. All of them worked independently from each other to allow detection of errors, divergent interpretation or ambiguous items⁽¹¹⁾. A panel of two gastroenterologists, with command of English, evaluated the obtained Portuguese version to achieve a consolidated version without discrepancies. The protocol of research had a positive report from the Ethics Committee for Health of the Hospital of Braga and the Ethics Subcommittee for Life and Health Sciences (SECVS). All data were collected anonymously.

Patients' selection

From July to October 2016, outpatients over 18 years old attending Gastroenterology Department of *Braga's* hospital, with ODS diagnosis were invited to participate in the study. Healthy individuals, mostly patients accompanying persons, were randomly selected as control group. Exclusion criteria were previous colorectal surgery or cancer, Hirschsprung's disease and/or inability to answer the questionnaire. A written informed consent was obtained from those who agreed to participate.

Study design and data collection

It was a prospective, observational, and longitudinal study carried out at the Gastroenterology Department of *Braga* Hospital.

At baseline, there was a face-to-face interview. Socio-demographic and clinical data were collected⁽¹³⁾. The Renzi ODS score and the validated Portuguese version 2 of the Sort Form – 36 items (SF-36) were applied. SF-36 is a generic measure of health that is clear and easy to fill, with good psychometric properties⁽¹⁴⁻¹⁶⁾. It comprises 36 items considering two main components (physical and mental). Furthermore, it is not specific for any age or disease. Higher SF-36 scores define more favorable health status. After 2 or more weeks, patients were contacted by telephone for a second Renzi ODS score application. Three months later, patients were contacted by telephone for a third interview to apply the Renzi ODS score again and to assess clinical evolution. Clinical evolution was rated in a Global Perceiving Effect (GPE) score of seven categories: "Much better", "Better", "Somewhat better", "Unchanged", "Somewhat worse", "Worse" and "Much worse", in a scale ranging from 3 to -3, respectively.

Statistical analysis

There is no consensus on the number of patients required to run

a factor analysis, with rules of thumb varying from 4 to 10 subjects per variable, with a minimum of 100 subjects⁽¹⁷⁾. At least 50 patients are needed to assess reliability⁽¹¹⁾. Collected data were gathered in Statistical Package for Social Sciences (SPSS)[®] - version 23.0 and all statistical analysis was performed using this program. Normality of the variables was evaluated through Skewness and Kurtosis values (normality considered for values between -1 and 1), Kolmogorov-Smirnov test and Shapiro-Wilk test⁽¹⁸⁾. If not specified, statistical significance was accepted for $P < 0.05$. Acceptability depends on the proportion of Renzi-ODS score and SF-36 questionnaires with incomplete filling and missing items.

Methodological testing according COSMIN checklist

• Internal consistency

This measurement property evaluates the extent to which different items in a questionnaire are correlated, thus measuring the same concept⁽¹⁷⁾. A principal component analysis (PCA) was performed to assess the unidimensionality of the scale. The scree plot of eigenvalues was used to determine the number of components and items with factor loading < 0.5 were considered for deletion⁽¹⁹⁾. The homogeneity of the items is determined by Cronbach's α , item-total, and item-item correlations. Cronbach's α was calculated using a one-at-a-time deletion procedure to assess the impact of each item on internal consistency separately. Cronbach's α between 0.70 and 0.95 was considered an indicator of adequate homogeneity of the items⁽⁷⁾. Inter-item correlations should be under 0.7 and corrected item-total correlations should exceed 0.4^(17,20).

• Reliability

To evaluate reliability, a second interview with application of Renzi ODS score was conducted, after 2 weeks. It was independent from the first, as neither the patients nor the investigator were aware of the scores achieved in the initial evaluation. This time interval was considered appropriate since it is long enough to prevent recall bias and short enough to ensure that there were no changes in the construct to be measured⁽¹¹⁾. Since it is an ordinal score, simple kappa coefficient (κ) for each item and weighted quadratic kappa for the total score were assessed to evaluate test-retest reliability⁽²¹⁾. Kappa is "acceptable" when it is > 0.40 , "fair to good" if it is between 0.40 and 0.75 or "excellent" if it is > 0.75 ⁽²²⁾.

• Measurement error

Measurement error includes the systematic and random error of a patient's score that is not attributed to true changes in the construct to be measured⁽¹¹⁾. The Standard Error of Measurement (SEM) was calculated using the formula $SEM = SD \sqrt{1-r}$ (SD =standard deviation; r =reliability). The Smallest Detectable Change (SDC) reflects the smallest individual change in score that can be interpreted as a real change in score, above measurement error, in one individual ($SDC_{ind} = SEM \times 1.96 \times \sqrt{2}$) and in a group of people ($SDC_{group} = SDC_{ind} / \sqrt{n}$)⁽¹⁷⁾.

• Content validity

Content validity was defined as the degree to which the content of a questionnaire is an adequate reflection of the construct to be measured and it should be assessed by judging the relevance and comprehensiveness of the items⁽²³⁾. An indication that the comprehensiveness of the items was assessed could be the indication of missed items: large floor and ceiling effects can indicate a scale that is not comprehensive⁽¹¹⁾.

• Validity (construct validity and structural validity)

This measurement property refers to the extent to which scores, in a particular instrument, relate to other measures and its consistency with theoretically derived hypotheses concerning the concepts that are being measured⁽¹⁸⁾. It includes structural validity and construct validity. Structural validity is evaluated by performing exploratory factor analysis, more specifically PCA (see Internal Consistency above). Construct validity was assessed using the ‘hypotheses testing’ method that tests predefined hypothesis, for example, expected correlations between measures or expected differences in scores between groups⁽¹⁷⁾. A higher percentage of correct predictions indicates stronger support for construct validity. Convergent evidence was assessed by calculating Spearman rank correlation coefficient between the scores of the Renzi ODS score and the SF-36, obtained at the first interview, based on the assumption that patients with more severe ODS would have lower quality of life; therefore it is expected a negative correlation, at least moderate, between the total Renzi ODS score and the total, physical and mental scores of SF-36⁽⁹⁾. A Spearman’s correlation <0.30 is classified as “weak”, between 0.30 and 0.50 as “moderate” and >0.50 as “strong”⁽²⁴⁾. As Renzi score showed significant differences between the median score for patients (median=4.5) and controls (median=12.5)⁽⁹⁾, it is expected a difference of, at least, 6 points between the Renzi ODS scores of the two groups.

• Responsiveness

Responsiveness is the ability of a questionnaire to detect clinically important changes over time in the construct to be measured, even if these changes are small, considering it a measure of longitudinal validity^(11,17). To evaluate responsiveness, a third interview was conducted by telephone, 3 months after the first one, to apply Renzi ODS score, under the same instructions and by the same initial interviewer, and to apply a GPE score to assess patient’s perceived change about the construct that are being measured. This time interval was considered appropriate since it is long enough to expect clinical change in patients with ODS, but still short enough to assume that patients would be able to recall whether any changes in their condition occurred during this period⁽²⁵⁾. It is expected that changes in Renzi ODS score between the first and the third interview negatively correlates with the GPE score with a correlation coefficient <-0.5⁽¹⁷⁾.

• Interpretability

Interpretability is defined as the degree to which one can assign qualitative meaning to quantitative scores⁽¹¹⁾. This can be assessed through distribution of the total scores in the study population and relevant subgroups, floor and ceiling effects and Minimal Important Change (MIC). Floor and ceiling effects are considered to be present if more than 15% of respondents achieved the lowest or highest possible score, respectively⁽¹⁷⁾. Study sample was dichotomized, according to GPE, in groups of “importantly improved” (includes “much better” and “better” options) versus “stable” (includes “somewhat better”, “unchanged” and “somewhat worse” options). Subsequently, receiver operating characteristic (ROC) analyses were performed. The area under the curve (AUC), a measure of responsiveness, was considered as the probability of correctly classifying the “importantly improved” from “stable” patients, and a good discrimination is considered if AUC >0.70^(17,26). For determining MIC, optimum ROC cut-off point of the change score was obtained by weighting sensitivity and

specificity equally. MIC for improvement was calculated instead of MIC for deterioration because one of the main goals of Renzi ODS score is to assess change after treatment interventions. If the measurement error (SDC) is smaller than MIC, it is possible to distinguish clinically important change from measurement error with much confidence^(17,27).

RESULTS

The gastroenterologists compared the two translated versions and the original version and no changes were applied to the final translation. A total of 113 individuals signed the consent and participated in the study with no missing items in the questionnaire. From the total of 113 individuals interviewed at baseline, 77 (68.14%) enrolled the patient’s group. The patients’ group had more women ($P<0.05$). No other significant differences were found between patients and controls.

Internal consistency

After performing PCA, one leading eigenvalue emerged in the scree plot of eigenvalues (FIGURE 2) that explained 53.37% of total variance, conferring unidimensionality to the scale. This means that all items are associated to a single construct. All items analyzed had factor loadings >0.5, which means high correlation with the principal component, so all items were kept. This was also taken into account when assessing structural validity.

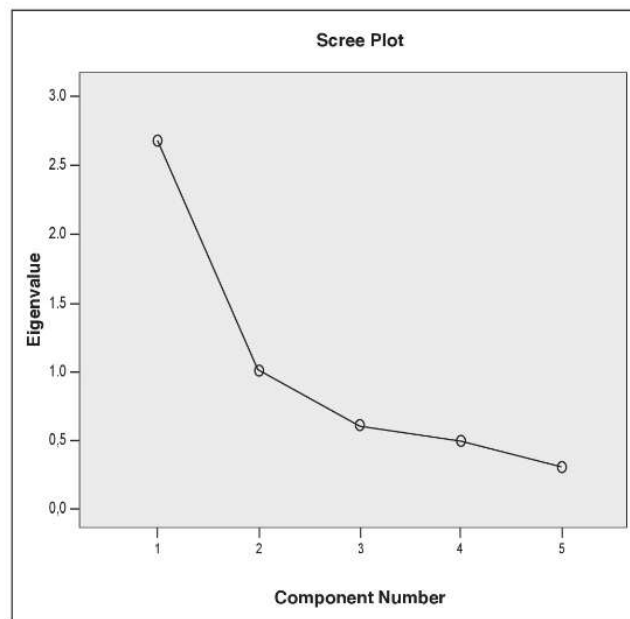


FIGURE 2. Scree plot of eigenvalues from PCA (n=113).

Cronbach’s α coefficient calculated for the 5 items was 0.77, thus all items have enough homogeneity (TABLE I). Cronbach’s α was also calculated considering deleting each item separately, which resulted in a range of 0.68 to 0.78, therefore the exclusion of any item would not substantially affect reliability. There is no redundancy between the items since inter-item correlations were <0.7. Corrected item total correlation lowest value was 0.39, which it’s not considerably different from 0.40.

TABLE 1. Cronbach's α coefficient for total Renzi ODS score, item-total correlation and Cronbach's α with item deleted for each item

Cronbach's α coefficient (n=113)	0.77	
	Item-total correlation	Cronbach's alpha if item deleted
1. Excessive straining	0.69	0.68
2. Incomplete rectal evacuation	0.68	0.68
3. Use of enemas and laxatives	0.41	0.78
4. Vaginal-anal-perineal maneuvers to attempt defecation	0.39	0.78
5. Abdominal discomfort/pain	0.57	0.72

Reliability

TABLE 2 shows the results of test-retest reliability, evaluated in 77 patients. As simple values for each item ranges from 0.49 to 0.81 and weighted quadratic kappa for the total score is 0.89, test-retest reliability is considered good to excellent.

TABLE 2. Descriptive statistics, test-retest reliability and measurement error of Renzi ODS score

Test Mean (SD) (n=77)	12.0 (\pm 2.9)
Re-test Mean (SD) (n=77)	12.4 (\pm 3.3)
Difference test-retest mean (SD) (n=77)	-0.35 (\pm 1.4)
Simple kappa coefficient (n=77)	
1. Excessive straining	0.75
2. Incomplete rectal evacuation	0.49
3. Use of enemas and laxatives	0.73
4. Vaginal-anal-perineal maneuvers to defecate	0.81
5. Abdominal discomfort/pain	0.71
Weighted quadratic kappa (n=77)	
Total score (95 CI)	0.89 (0.85 - 0.94)
SEM (95% CI)	0.96 (0.71-1.12)
SDCind (95% CI)	2.66 (1.97-3.10)
SDCgroup (95% CI)	0.30 (0.22-0.35)

CI: confidence interval; SD: standard deviation; SDCind: Smallest Detectable Change at the individual level; SDCgroup: smallest detectable change at group level; SEM: standard error of measurement.

Measurement error

SDC at the individual level was 2.66 and at the group level was 0.30 (TABLE 2).

Validity

As previously hypothesized, the total score of Renzi ODS score negatively correlated with the total ($r_s=-0.32$; $P<0.01$) and physical scores ($r_s=-0.43$; $P<0.01$) and these are considered moderate correlations. There was also a negative correlation with mental scores of SF-36 ($r_s=-0.14$) but it did not reach statistical significance (TABLE 3). Significant differences were obtained (Mann-Whitney U test=0; $P<0.01$) comparing patients (median=12) and controls (median=1). Therefore, there is a difference of 11 points in the medians of both groups, greater than the 6 point previously hypothesized.

TABLE 3. Spearman's correlation coefficients determined when comparing Renzi ODS score and SF-36's scores

	SF-36 total score	SF-36 physical score	SF-36 mental score
Renzi ODS score (n=77)	-0.32*	-0.43*	-0.14

*Correlation statistically significant ($P<0.01$).

Responsiveness

There was a negative correlation between change score in Renzi ODS score and the GPE score with a correlation coefficient <-0.5 ($r_s=-0.86$; $P<0.01$). Hypothesis regarding ROC analysis was confirmed, since AUC was 0.97 (95% CI: 0.91-1.00).

Interpretability

Neither floor nor ceiling effects were observed for any of the scores (TABLE 4). Using ROC analysis for discriminating improved versus stable patients (as assessed by the GPE score) through changes in the Renzi ODS score and by weighting sensitivity and specificity equally, the best cut-off was 2.00 (sensitivity-100%; specificity-92%). SDCgroup is smaller than MIC (0.30<2.00) and SDCind is greater than MIC (2.66>2.00).

DISCUSSION

Nowadays, ODS is still a common but complex syndrome. A clinical severity index, as proposed by Renzi et al. could be a useful tool in the diagnostic algorithm and the evaluation of meaningful changes after treatment⁽⁹⁾.

Since Renzi ODS score was successfully validated in the English language, showing good discriminatory power to distinguish between patients and controls and changes in patients over time, we intend to validate a Portuguese version of Renzi ODS score following COSMIN checklist guidelines^(9,11).

According to what we stated, we could validate the domains of reliability, validity, responsiveness and interpretability (at group level) of Renzi ODS score, following strict methodology based in the COSMIN checklist⁽¹¹⁾.

Regarding cross cultural validity, guidelines for a correct translation and cultural adaptation were fulfilled without considerable constraints, since it is a pretty straightforward questionnaire⁽¹²⁾. Good acceptability and absence of missing items reinforced this.

The results showed good internal consistency assessed by PCA procedure, confirming that this is a unidimensional scale. The reliability of Renzi ODS score was confirmed by high internal consistency (Cronbach's $\alpha=0.77$ supporting homogeneity of all items in the scale), test-retest (weighted quadratic kappa $\kappa=0.89$) and inter-rater (0.96) reliabilities.

Validity was assessed through structural validity and hypothesis testing. Structural validity refers to PCA, already explained above. Of the following a-priori-formulated hypotheses in correlation analysis: the Renzi ODS score is negatively and moderately correlated with the total and physical scores of SF-36 ($r_s=-0.32$ and -0.43, respectively). Although also negatively correlated, the same assumption failed on the statistical association of Renzi ODS score with mental score of SF-36. Probably, a greater study sample, as it was used in the original validation study, would lead to a more significant correlation values⁽⁹⁾. There was a significant

TABLE 4. Distribution of total scores, floor and ceiling effects

	Mean	SD	Median	Range	Floor effects	Ceiling effects
Renzi ODS score at first interview (n=113)	8.71	5.51	10.00	0.00-19.00	9 (7.96%)	0
Female (n=78)	10.63	4.44	12.00	0.00-18.00	-	-
Male (n=35)	4.43	5.29	2.00	0.00-19.00	-	-
Renzi ODS score at second interview (n=77)	12.39	3.27	13.00	5.00-19.00	0	0
Female (n=66)	12.55	3.18	13.00	5.00-19.00	-	-
Male (n=11)	11.46	3.83	11.00	6.00-19.00	-	-
Renzi ODS score at third interview (n=30)	12.10	4.11	12.50	4.00-20.00	0	1 (3.33%)
Female (n=27)	12.56	4.02	13.00	4.00-20.00	-	-
Male (n=3)	8.00	2.65	7.00	6.00-11.00	-	-
SF-36 at first interview (n=77)	48.42	16.71	43.61	19.72-87.17	0	0
Female (n=66)	47.51	16.61	43.06	19.72-85.50	-	-
Male (n=11)	53.85	17.06	52.72	34.44-87.17	-	-

SD: standard deviation.

difference between the median of Renzi ODS score considering patients and controls, being this difference greater than the 6 points previously hypothesized.

Responsiveness was assessed by a similar fashion as construct validity, but in this case, hypothesis about correlation of Renzi ODS score changes with GPE score were formulated, considering an “anchor based” method. A correlation coefficient <-0.5 was obtained, as expected. AUC was 0.97, supporting a good responsiveness of Renzi ODS score. SDCind >2.66 can be considered real changes at the individual level and large SDCind values in the current study are somewhat expected, suggesting questionnaire’s inability to detect minimal but still clinically important changes. Changes in SDCgroup >0.30 can be detected with 95% confidence.

Interpretability considered assessment of floor and ceiling effects, and none of them were observed in any of the administrations of Renzi ODS score. A MIC of 2,00 was defined for discriminating “importantly improved” patients. Comparing measurement error with MIC, MIC is higher than SDCgroup and smaller than SDCind, implying that Renzi ODS score is ineffective at detecting minimal, but still clinically important changes at individual level⁽²⁷⁾. Thus, in future studies, the sample size should be adjusted accordingly to minimize measurement error.

Although the main goal of this work was achieved, there are some limitations. In the original validation of ODS score, Renzi et al. used 100 patients and 100 controls, which is considerably greater than the sample size used by us. A greater sample size, would strengthen statistical analysis in the validation of the score and would probably minimize measurement error, in order to achieve interpretability at the individual level⁽²⁷⁾. An even better option would be a multicentric study in order to validate a score culturally well adapted to the Portuguese population. Questionnaires applied at baseline were done by

face-to-face interview and score application at 2 weeks and 3 months occurred by telephone. Although applied by the same interviewer under the same instructions, this might lead to bias on the obtained scores⁽¹¹⁾. Anchor based methods, resorting a GPE scale, used to analyze responsiveness validity and to achieve MIC value, was reported as a reliable and valid measure of health change perceived by patients and considered the best measure from individual perspective. However, a retrospective rating of change obtained over an extended period of time are susceptible to recall bias^(28,29). Furthermore, the 3 months’ follow-up to evaluate clinical perceived change by patients is probably not enough, since this is a chronic disability which may not change much in such a short period of time.

CONCLUSION

According to COSMIN checklist, a validated Portuguese version of ODS score was developed, showing good internal consistency, content and construct validity, responsiveness and interpretability, at the group level. So, Renzi ODS score arises as a simple and concise instrument, designed to be a preliminary tool to approach patients with ODS, to help diagnose and grade ODD severity, and to evaluate treatment effectiveness more precisely.

Authors’ contributions

Caetano AC and Rolanda C were involved in the study concept and design; Caetano AC and Dias S were involved in the acquisition of data and completed the analysis and interpretation of data; Santa-Cruz S reviewed the statistical analysis; Caetano AC and Dias S contributed to the drafting of the manuscript; Rolanda C and Santa-Cruz A made a critical revision and English editing of the manuscript.

Caetano AC, Dias S, Santa-Cruz A, Rolanda C. Score de Renzi para distúrbios evacuatórios – validação da versão portuguesa de acordo com a checklist COSMIN. *Arq Gastroenterol.* 2018;55(1):55-60.

RESUMO – Contexto – Recentemente, o Score de Distúrbios Evacuatórios (SDE) foi desenvolvido e validado por Renzi para avaliação e comparação da eficácia do tratamento dos doentes com esta patologia. **Objetivo** – O nosso objetivo é validar uma versão portuguesa do SDE de acordo com as orientações da checklist de COSMIN. **Métodos** – O SDE foi traduzido para o português, cumprindo as orientações para validação cultural. Indivíduos com distúrbio evacuatório e controlos saudáveis foram convidados a responder ao SDE numa fase inicial, 2 semanas e 3 meses depois, respetivamente. Foi avaliada a consistência interna, confiabilidade, erro de medição, validade de conteúdo e constructo, responsividade e interpretabilidade. **Resultados** – Foram entrevistados 113 indivíduos (77 doentes; 36 controlos saudáveis) na fase inicial. O SDE foi aplicado novamente aos 77 doentes, 2 semanas depois, e a 30 doentes, 3 meses depois. Relativamente à consistência interna, a análise fatorial confirmou a unidimensionalidade e o coeficiente α de Cronbach foi 0,77, suportando homogeneidade dos itens. O kappa quadrático ponderado de 0,89 estabeleceu a reprodutibilidade teste-reteste. Considerando o erro de medição, a mudança mínima detectável a nível individual foi 2,66 e a nível de grupo foi 0,30. A validade do constructo foi avaliada através do coeficiente de correlação de Spearman entre o SDE e o score total (-0,32) e físico (-0,43) do SF-36. Em termos de validação clínica, verificou-se uma diferença significativa de 11 pontos entre as médias dos doentes e controlos. A responsividade foi confirmada pelo coeficiente de correlação de -0,86 entre a mudança do score e a evolução clínica, avaliados após 3 meses. Através da curva ROC, a mudança mínima importante foi 2,00 e a AUC foi 0,97. Não foram observados efeito-chão efeito-tecto. **Conclusão** – Este projeto permitiu validar a versão portuguesa do SDE de Renzi. É possível agora utilizar esta ferramenta na avaliação de distúrbios evacuatórios em doentes falantes de língua portuguesa.

DESCRITORES – Constipação intestinal, classificação. Defecação. Psicometria. Inquéritos e questionários.

REFERENCES

1. Bharucha A, Pemberton J, Locke III G. American Gastroenterological Association Technical Review on Constipation. *Gastroenterology.* 2013;144:218-38.
2. D'Hoore A, Penninckx F. Obstructed Defecation. *Semin Colon Rectal Surg.* 2003;22:45-9.
3. Mearin F, Ciriza C, Mínguez M, Rey E, Mascort JJ, Peña E, et al. Clinical Practice Guideline: Irritable bowel syndrome with constipation and functional constipation in the adult. 2016;108:332-61.
4. Rosen A. Obstructed defecation syndrome: Diagnosis and therapeutic options, with special focus on the STARR procedure. *Isr Med Assoc J.* 2010;12:104-6.
5. Chiarioni G, Kim SM, Vantini I, Whitehead WE. Validation of the Balloon Evacuation Test: Reproducibility and Agreement With Findings From Anorectal Manometry and Electromyography. *Clin Gastroenterol Hepatol.* Elsevier, Inc; 2014;12:2049-54.
6. Halverson A, Orkin B. Which physiologic tests are useful in patients with constipation? *Dis Colon Rectum.* 1998;41:735-9.
7. Rao SSC, 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;16:589-96.
8. 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. *Color Dis.* 2008;10:84-8.
9. Renzi A, Brillantino A, Di Sarno G, D'Aniello F. Five-Item Score for Obstructed Defecation Syndrome: Study of Validation. *Surg Innov.* 2013;20:119-25.
10. 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;39:681-5.
11. Mookink L, Terwee C, Patrick D. The COSMIN checklist manual. 2009;1-8.
12. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine (Phila Pa 1976).* 2000;25:3186-91.
13. Steele SR, Mellgren A. Constipation and obstructed defecation. *Clin Colon Rectal Surg.* 2007;20:110-7.
14. Ferreira PL. Criação da versão Portuguesa do MOS SF-36. Parte II - Testes de validação. *Acta Med Port.* 2000;13:119-27.
15. Hawthorne G, Osborne RH, Taylor A, Sansoni J. The SF36 Version 2: Critical analyses of population weights, scoring algorithms and population norms. *Qual Life Res.* 2007;16:661-73.
16. Ware JE SS. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Med Care.* 1992;30:473-81.
17. Terwee CB, Bot SDM, de Boer MR, van der Windt DAWM, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol.* 2007;60:34-42.
18. Chan YH. Biostatistics 101: Data presentation. *Singapore Med J.* 2003;44:280-5.
19. Floyd F, Widaman K. Factor analysis in the development and refinement of clinical assessment instruments. *Psychol Assess.* 1995;7:286-99.
20. Gliem JA, Gliem RR. Calculating, interpreting, and reporting Cronbach's alpha reliability coefficient for Likert-type scales. *Midwest Res to Pract Conf Adult, Contin Community Educ.* 2003;82-8.
21. Brenner H, Kliebsch U. Dependence of weighted kappa coefficients on the number of categories. Vol. 7, *Epidemiology (Cambridge, Mass.).* 1996. p. 199-202.
22. Hernaez R. Reliability and agreement studies: a guide for clinical investigators. *Gut.* 2015;64:1018-27.
23. Mookink LB, Terwee CB, Knol DL, Stratford PW, Alonso J, Patrick DL, et al. The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: a clarification of its content. *BMC Med Res Methodol.* 2010;10:22.
24. Cohen J. *Statistical power analysis for the behavioral sciences.* Hillsdale, New Jersey Lawrence Erlbaum Assoc Inc. 1988.
25. Thorborg K, Hölmich P, Christensen R, Petersen J, Roos EM. The Copenhagen Hip and Groin Outcome Score (HAGOS): development and validation according to the COSMIN checklist. *Br J Sports Med.* 2011;45:478-91.
26. Heidemann CH, Godballe C, Kjeldsen AD, Charlotte E, Johansen J, Faber CE, et al. The Otitis Media-6 questionnaire: psychometric properties with emphasis on factor structure and interpretability. *Health Qual Life Outcomes.* 2013;11:10.
27. Terwee CB, Roorda LD, Knol DL, De Boer MR, De Vet HCW. Linking measurement error to minimal important change of patient-reported outcomes. *J Clin Epidemiol.* Elsevier Inc. 2009;62:1062-7.
28. Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. 2003;56:395-407.
29. De Boer MR, De Vet HCW, Terwee CB, Moll AC, Völker-Dieben HJM, Van Rens GHMB. Changes to the subscales of two vision-related quality of life questionnaires are proposed. *J Clin Epidemiol.* 2005;58:1260-8.



CHAPTER 6

Caetano AC, Costa D, Gonçalves R, Correia-Pinto J, Rolanda C. *Does sequential balloon expulsion test improve the screening of defecation disorders?* BMC Gastroenterol. 2020 Oct 14;20(1):338.

RESEARCH ARTICLE

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Does sequential balloon expulsion test improve the screening of defecation disorders?

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Abstract

Background: A defecation disorder (DD) is a difficulty in evacuation documented by physiological exams. However, this physiological evaluation can be cumbersome, inaccessible and costly. Three “low-cost” tools to evaluate DD—a clinical DD score, the balloon expulsion test (BET) and a digital rectal examination (DRE) score were evaluated as separate or combined tests for DD screening.

Methods: This prospective study occurred between January 2015 and March 2019 in the Gastroenterology Department of a tertiary hospital. Besides the gold standard physiological tests, constipated patients answered the clinical DD score and were evaluated by DRE and BET [standard and variable volume (VV)].

Results: From 98 constipated patients, 35 (38.9%) were diagnosed with DD according to Rome IV criteria, mainly female ($n = 30$, 86%) with a median age of 60 years old. The clinical DD score revealed an AUC of 0.417 (SE = 0.07, $p = 0.191$). The DRE score displayed an AUC of 0.56 (SE = 0.063, $p = 0.301$). The standard BET displayed a sensitivity of 86%, specificity of 58%, positive predictive value (PPV) of 57% and negative predictive value (NPV) of 86%. The sequential VVBET followed by standard BET improved the BET performance regarding the evaluation of DD, with a sensitivity of 86%, specificity of 67%, PPV of 63% and NPV of 87%. The sequential BET had an OR 8.942, $p > 0.001$, CI 3.18–25.14, revealing to be the most significant predictor for DD screening.

Conclusion: The sequential BET is a low cost, well-performing DD screening tool, appropriate to the Primary Care Setting.

Keywords: Constipation, Defecation disorders, Low-cost tools

Background

A defecation disorder (DD) is defined as a difficulty in evacuation or emptying the rectum. DD may result from impaired anorectal function or rectal structural disturbances in patients with complaints of Chronic Constipation (CC) [1–3].

DD was recently defined by the Rome IV criteria, based on symptoms and objective physiological criteria—Table 1 [4, 5]. Therefore, the diagnosis of DD is established when a patient with functional chronic

constipation (CC) or irritable bowel syndrome with constipation (IBS-C) has impaired evacuation as demonstrated by 2 of 3 types of tests—balloon expulsion test (BET); imaging (conventional defecography, dynamic ultrasound or dynamic magnetic resonance); anorectal manometry (ARM) or electromyography (EMG). This physiological evaluation is not always easily accessible, moreover it can be long and costly [3, 6, 7]. American studies report costs of healthcare utilization for CC as high as 500 dollars-patient-year while the exact impact of CC diagnostic assessment and treatment in Western Europe healthcare systems is unknown [8].

Thus, there is a subgroup of constipated patients—with DD—that can benefit from specific treatment behind laxatives, and we do not want them to miss proper treatment

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Table 1 Rome IV diagnostic criteria for functional defecation disorders**Rome IV Diagnostica criteria (a) for functional defecation disorders**

1. The patient must satisfy diagnostic criteria for functional constipation and /or Irritable Bowel Syndrome with constipation
 2. During repeated attempts to defecate, there must be features of impaired evacuation, as demonstrated by 2 of the 3 following 3 tests:
 - a. Abnormal balloon expulsion test
 - b. Abnormal anorectal evacuation pattern with manometry or anal surface electromyography
 - c. Impaired rectal evacuation by imaging
- (a) Criteria fulfilled for the last 3 months with symptoms onset at least 6 months before diagnosis

Table 2 Renzi clinical DEFECATION DISORDERS Score

Symptoms/score	0	1	2	3	4
Excessive straining	Never	Rarely	Sometimes	Usually	Always
Incomplete rectal evacuation	Never	Rarely	Sometimes	Usually	Always
Use of enemas/laxatives	Never	Rarely	Sometimes	Usually	Always
Vaginal/Perineal digital pressure	Never	Rarely	Sometimes	Usually	Always
Abdominal discomfort/pain	Never	Rarely	Sometimes	Usually	Always

Never, never; rarely, < 1/month; sometimes, < 1/week, ≥ 1/month; usually, < 1/day; ≥ 1/week; always, ≥ 1/day

in consequence of the DD underdiagnosis. However, with the nowadays cost-effectiveness constraints, it may be impossible to perform the recommended physiological evaluation to all patients seeking a medical consultation for CC or IBS-C. A cheaper but satisfactory screening approach of DD that promotes an adequate selection of complementary tests and an earlier and adequate treatment seems ideal. Applying the creative concept of “low-cost” tools, we run an extensive review of the subject [9]. We found 3 potential “low-cost” tools—a DD clinical score, the BET and the digital rectal examination (DRE). Based on current evidence, it is not possible to know whether these “low-cost” strategies are useful in this setting [9].

Going into detail, no clinical score has emerged as a relevant diagnostic method in the diagram of DD and none was evaluated as a screening tool. Two specific DD scores (Altomare score and Renzi score) were validated to grade severity and value of treatment’s efficacy [10, 11]. Two important limitations prevented us from using Altomare score—it includes “time spent at the toilet” and “stool consistency”, items with a strong cultural influence and diet effect. The Renzi score is a 5-items score (Table 2) that assesses various complains of an abnormal evacuation and shows less cultural impact. The BET is a convenient procedure but described with inconsistent methodology especially regarding the volume used to inflate the balloon [9, 12–14]. Considering the physiological aspects of defecation, there remains doubts if

a fixed low intrarectal volume is enough to trigger the desire to defecate or if higher variable volumes associated with the constant desire to evacuate can compensate for rectal hiposensitivity [2, 12]. The DRE is another low-cost tool that may sometimes be under or inappropriately used [15–17] and its value in DD was assessed in very few studies [9]. Only Tantiplachiva proposed a DRE score to diagnose DD [18]. Therefore, there is a need for prospective studies with descriptive and consistent methodology to evaluate BET and DRE utility. In addition, it seems crucial an external validation of the few studies published so far [11, 12, 18]. Furthermore, no study in the literature evaluated a clinical DD score (or combination of its individual items) and these “low-cost” physiological tests—BET and DRE score. This effort seems relevant in the screening of DD in primary health care but also with potential utility in the diagnosis and assessment of treatment’s efficacy. This strategy may generate clear clinical and financial advantages [1, 2]. The aim of this study was to evaluate the performance of the “low-cost” tests in the screening of DD as separate or combined tools.

Methods

Study design and subjects

This was a cross-sectional study. Consecutive patients with CC or IBS-C (Rome IV criteria), followed in the Department of Gastroenterology of Braga Hospital between January 2015 and March 2019 were prospectively proposed to the study protocol. The exclusion criteria were previous colonic and anorectal surgery, inflammatory bowel disease, colorectal cancer, anal cancer, other secondary causes of constipation, anorectal abnormalities that would influence symptoms of defecation detected by proctologic examination as anal fissure and haemorrhoids, incapacity to understand the study protocol.

During the clinical interview, the Renzi DD score was applied, followed by the DRE and the BET protocol, always by the same operator, as described in the next sections. The gold standard physiological tests (in our department anorectal manometry and defecation

imaging) were subsequently scheduled and performed by another operator blinded to the study. A positive diagnosis of DD was considered according to 2 criteria of Rome IV, excluding information from the BET. Our constipated patients with no DD according with the current standards of diagnosis served as control group. Thus, patients with a positive BET plus a positive ARM or defecography were not included in DD group and were excluded from the control group (NoDD).

The Ethics Committee for Health of the Hospital of Braga approved the research protocol. Written informed consent was obtained from all participants. All data were collected anonymously and Portuguese regulations applicable to the management of personal data were followed at all times.

Renzi DD score

A clinical DD score developed and validated by Renzi, as described in introduction and shown in Table 2, is divided in 5 items—excessive straining, incomplete rectal evacuation, use of enemas/laxative, vaginal/perineal digital pressure, abdominal discomfort/pain—that are scored from 0 to 4 points according to its frequency in everyday patients' life. A final score ≥ 9 points was assumed as abnormal [11]. We validated the Portuguese version of the score [19] according to the Consensus based Standards for the selection of the Health Measurement Instruments (COSMIN) checklist [20] and following guidelines for cross-cultural validity [21]. The score was applied in a face to face interview. In this study, the score was also deconstructed and evaluated in diverse combinations of items.

DRE technique

The general DRE was performed according to the technique described by Talley [15]. It was followed by the specific tests for pelvic floor dysfunction: the patient was requested to strain and try to push out the finger (to assess paradoxical external anal sphincter and puborectalis contraction), then the patients was asked regarding pain when pressing the posterior rectal wall (to assess puborectalis muscle tenderness) and then a hand was placed on the anterior abdominal wall of the patient while asking him/her to strain again (to assess if the patient is excessively contracting the abdominal wall). The DRE was performed always by the same examiner (the main investigator) who knew the patients previously from the outpatient consultation. Next, we applied the Tanthiplachiva score defining a positive diagnosis of DD when two of the following criteria were present: (1) paradoxical anal contraction or impaired anal relaxation, (2) impaired push effort, (3) absence of perineal descent [18].

BET technique

With the patient lying in the left lateral position, an empty 4 cm long balloon covered with lubricating jelly and tied to a flexible catheter (external diameter, 6 mm) was placed in the rectum. The balloon was then filled with 50 ml of air through the catheter. The patient was asked to expel the balloon. A stop-watch was started and stopped when the patient expelled the device. The time taken for expelling the balloon was recorded. An abnormal BET (standard BET) was defined as inability to expel the balloon in less than 1 min. A second BET was performed following the same steps but with a variable volume of air—the volume of air associated with a constant desire to evacuate (vvBET).

Statistical evaluation

Continuous data is presented as median and interquartile range. Normal distribution was checked using skewness and kurtosis. Comparisons among groups were carried out using the Chi-square test or Mann–Whitney test. The ROC curves were used to evaluate the performance of the continuous variables (clinical DD score and DRE score). Sensitivity and specificity were calculated for the abnormal clinical score, altered DRE, abnormal standard BET, abnormal vvBET and abnormal sequential BET. Candidate variables for inclusion in a prediction model were any significant (or borderline significant) variables at univariate analysis or variables whose inclusion was supported by the existing literature. Potential predictors were identified using backward stepwise selection. p values < 0.05 was defined for rejection of the null hypothesis. All the statistical analyses were conducted using the software SPSS 22.0 (IBM, USA).

Results

From 98 patients with the clinical criteria of CC, 8 were excluded because there was not enough data to admit or exclude the DD or NoDD diagnosis. Thirty-five patients (38.9%) were diagnosed with DD, mainly female ($n = 30$, 86%) with a median age of 60 years old. The 55 constipated patients without criteria for DD (NoDD) were also mainly female ($n = 51$, 93%) but with a median age of 51 years old ($p = 0.009$). Table 3 describes demographic and clinical characteristics of the patients.

Renzi DD score

Regarding clinical complaints, excessive straining, was reported as usually or always by 64.7% of the DD patients and by 63.6% of the NoDD patients. Only 3 DD patients refer never perform excessive straining in evacuation and no patient of the NoDD group refer never perform excessive straining. Regarding

Table 3 Patients demographic and clinical characteristics

Characteristics	DD group	NoDD group	<i>p</i>
Age (years)	60	51	0.009
Gender (fem/male)	30/5	51/4	0.28
Total Renzi score	11	11	0.452
ARM rest pressure (mmHg)	62	63	0.792
ARM sustained pressure (mmHg)	101	105	0.805
ARM minimal sensitivity (ml)	97	96	0.991
ARM sustained sensitivity (ml)	203	192	0.668
ARM maximal sensitivity (ml)	242	221	0.302
Presence of anal defects	3	2	
Presence of structural abnormalities	18	12	

ARM anorectal manometry

incomplete rectal evacuation, 61.8% of the DD patients and 69% of the NoDD patients complain to feel it usually or always. Again only 2 patients in the DD group and 1 patient in the NoDD group describe never feel incomplete rectal evacuation. Regarding the use of enemas or laxatives, 48.5% of the DD patients refer to use it usually or always as well as 56.3% of the NoDD patients. Only 14.5% of the NoDD patients and 27.3% of the DD patients refer never use it. The vaginal/perineal digital pressure was usually or always used by 29.4% of the DD patients and by 16.3% of the NoDD patients; 52.9% of the DD patients and 43.9% of the NoDD patients refer never to require it. Abdominal discomfort or pain was felt usually or always by 34% of the DD patients and by 40% of the NoDD patients. Four patients in both groups never felt abdominal pain.

The clinical DD score was abnormal in 89% of the NoDD patients and in 64.7% of patients with DD ($p=0.04$). Regarding each individualized item of the clinical DD score there were no significant differences between the groups ($p>0.05$). The abnormal clinical DD score (score ≥ 9 points) displayed a sensitivity of 65%, specificity of 10%, positive predictive value (PPV) of 31% and negative predictive value (NPV) of 33%. It revealed an AUC of 0.417 (SE = 0.07, $p=0.191$).

DRE technique

Regarding the DRE, paradoxical anal contraction or impaired anal relaxation was identified in 31.4% of the DD patients and in 16.3% of the NoDD patients ($p=0.094$). Impaired push effort was recognized in 34.3% of the DD patients and in 23.6% of the NoDD patients ($p=0.272$). The absence of perineal descent was documented in 28.6% of the DD patients and in 27.3% of the NoDD patients ($p=0.893$).

The DRE was abnormal in 18.2% of the NoDD patients and in 28.6% of DD patients ($p=0.248$). The abnormal clinical DD score displayed a sensitivity of 29%, specificity of 82%, PPV of 50% and NPV of 64%. The DRE score displayed an AUC of 0.56 (SE = 0.063, $p=0.301$).

BET technique

The standard BET was abnormal in 41.8% of the NoDD patients and in 85.7% of DD patients ($p<0.001$). Evaluating the vvBET, the median volume of the BET associated with a constant desire to evacuate was 133.2 ± 60.9 ml. The vvBET was abnormal in 32.7% of the NoDD patients and in 82.9% of DD patients ($p<0.001$). The performance of the BET using fixed volume and variable volume was different in 6 patients—5 patients were capable of expelling the variable-volume balloon (normal vvBET) but not the fixed-volume balloon (abnormal standard BET) and one patient had the inverse performance.

The standard BET displayed a sensitivity of 86%, specificity of 58%, PPV of 57% and NPV of 86%. The vvBET alone showed a sensitivity of 83%, specificity of 67%, PPV of 62% and NPV of 86%. The sequential BET (vvBET followed by standard BET) improves the BET performance regarding evaluation of DD, with a sensitivity of 86%, specificity of 67%, PPV of 63% and NPV of 88%.

Tool to screen DD

Table 4 displays the performing characteristics of the “low-cost” tools under evaluation.

At univariate analysis, only age ($p=0.022$), standard BET ($p<0.001$), vvBET ($p<0.001$) and sequential BET ($p<0.001$) were significant predictors of DD. Logistic regression demonstrated that sequential BET had an

Table 4 Performance of the low-cost tools

Tool /performance measurement	Sensitivity	Specificity	PPV	NPV	Accuracy
Abnormal (> 9 points) clinical DD score	65	10	31	33	31
Abnormal (≥ 2 points) Digital rectal examination	29	82	50	64	61
FV BET (standard)	86	58	57	86	69
VV BET	83	67	62	86	73
Sequential BET (VV » FV)	86	67	63	88	75

DD defecation disorder, BET balloon expulsion test, VV variable volume, FV fixed volume, PPV positive predictive value, NPV negative predictive value

OR 8.942, $p > 0.001$, CI 3.18–25.14 and that the sequential BET stood out as the most significant predictor for screening DD.

Discussion

Chronic constipation is one of the five most common gastrointestinal disorders. It consumes substantial health care resources due to the high prevalence and specificity of the diagnostic tests and treatments involved [3, 7]. In the current times, with financial cutbacks in healthcare, the judicious use of technology seems to be a relevant issue [7, 22]. Taking all these aspects in consideration, we selected 3 “low-cost” tools in order to understand their role in the screening of DD as potential tools to be used in a first approach, namely in Primary Care Setting.

As shown in Table 3, demographic and clinical characteristics of both DD patients and NoDD patients are identical except for age as DD patients are significantly older (60 vs 51 years old), that is also reported in other series and can be explained by the cumulative structural and physiological alterations in the pelvic floor of older women. ^(1–3,6,23).

The Renzi clinical DD score, in the original study, showed good discriminatory power to distinguish between patients and controls (sensitivity 92% and specificity 96%) and also variations in patients over time [11]. However, in our study population, the clinical score did not perform well as a screening tool (sensitivity 65% and specificity 10%). In fact, Renzi et al. validated their score specifically to grade defecation disorders and not as a diagnostic tool among constipated patients. Besides their patients' sample was selected according to Rome III criteria and specific exclusion criteria—no irritable bowel syndrome and no slow transit constipation. That way it is difficult to reproduce their good results using their score as a screening tool. This goes in line with recent reviews that consider clinical scores useless for screening or diagnostic purposes in DD [24, 25]. One possible explanation is that patients, when asked about their symptoms, tend to exaggerate their complains when evoking them retrospectively. No item of the clinical DD score had a distinctive individualized performance, not even the most controversial item of the DD clinical score—“abdominal discomfort/pain”—pointing to the continuous spectrum of pain in the DD subgroup of these pathologies (IBS with constipation and CC).

The DRE score, similarly, did not perform well as a screening tool. Compared with the results presented by Tantiphlachiva in their sample of 209 patients (sensitivity of 75% and specificity of 87%), the DRE score had a poorer performance in our study population (sensitivity 29% and specificity 82%) [18]. The DRE is an operator-dependent technique. Although we tried to decrease this

bias with the execution of the DRE always by the same operator, we still have to take into account the years of professional experience of the main investigator (5 years) compared with the Tantiphlachiva team. It would be interesting to evaluate the learning curve of the DRE technique. Another possible bias is the cultural barrier—it is a dynamic evaluation, and different populations may not consistently perform the same oral instructions.

The standard BET performance (evaluation of the ability to evacuate solid stool) is in accordance with the majority of the data presented in the literature [9]. Trying to discriminate the best performance of the BET, besides the standard BET, we evaluated the vvBET (evaluation of rectal sensory function, which can also disturb evacuation ability). The sequential BET, where vvBET is followed by standard BET, improved the BET performance regarding evaluation of DD. These results points to the importance of rectal filling and its conscious awareness for a correct BET, improving the BET capability as a screening tool. Our results validate Minguez et al. results [12]. We also shared their enthusiasm that simple tools can be easily performed in any examination room and can be incorporated in the preliminary evaluation of patients with CC. The sequential BET increases specificity, PPV and NPV to this tool. Increasing age can also add specificity to the BET sequence. So, the sequential BET proposed could become an interesting tool for screening constipated patients in the Primary Care setting.

This study has some limitations already pointed out—cultural barrier regarding the patients, years of experience regarding the investigators. The left lateral position to perform the BET can also be seen as a limitation as the sitting position is more physiological [26]. The sample size can also be seen as a limitation. In our defense, while both the clinical score and the DRE score did not reveal discriminative power to screen constipated patients, the standard BET had a similar performance to that reported by other series [9]. Besides, as we know, an algorithm or score always performs better in the validation population (reported in the original papers) and the consistency of the results when performing the external validation is often not achieved. Pursuing the refinement of the low-cost tools, the sequential BET seems the most suitable to potential use in the Primary Care Setting.

Conclusion

The clinical DD score and the DRE did not reveal discriminative power to evaluate patients with DD. The BET stands as a good, reproducible and low-cost tool, that performs better when sequentially used with variable volume and fixed volume. Age can improve the BET specificity to exclude DD.

Abbreviations

AUC: Area under the curve; ARM: Anorectal manometry; BET: Balloon expulsion test; CC: Chronic constipation; DRE: Digital rectal examination; DD: Defecation disorder; EMG: Electromyography; IBS-C: Irritable bowel syndrome-subtype constipation; ROC: Receiver Operating Characteristic; VV: Variable volume; PPV: Positive predictive value; NPV: Negative predictive value.

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Authors' contributions

ACC and CR were involved in the study concept and design; ACC and DC were involved in the acquisition of data and completed the analysis and interpretation of data; DC and RG reviewed the statistical analysis; ACC, DC and CR contributed to the drafting of the manuscript; JCP and CR made a critical revision and English editing of the manuscript. At the end of the process, all authors have read and approved the manuscript.

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Availability of data and materials

The data is available from the corresponding author in digital format that can be sent to the journal.

Ethics approval and consent to participate

The Ethics Committee for Health of the Hospital of Braga approved the research protocol. Written informed consent was obtained from all participants. All data were collected anonymously and Portuguese regulations applicable to the management of personal data were followed at all times.

Consent to publish

The authors give their consent to publish.

Competing interests

We declare there is no conflict of interest or disclosure to formulate.

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References

- Bharucha AE, Pemberton JH, Locke GR. American gastroenterological association technical review on constipation. *Gastroenterology*. 2013;144(1):218–38.
- Bharucha AE, Rao SSC. An update on anorectal disorders for gastroenterologists. *Gastroenterology*. 2014;146(1):37–45.
- Carrington EV, Scott SM, Bharucha A, et al. International anorectal physiology working group and the international working group for disorders of gastrointestinal motility and function. Expert consensus document: advances in the evaluation of anorectal function. *Nat Rev Gastroenterol Hepatol*. 2018;15(5):309–23.
- Schmulson MJ, Drossman DA. What is new in Rome IV. *J Neurogastroenterol Motil*. 2017;23(2):151–63.
- Simren M, Palsson OS, Whitehead WE. Update on Rome IV criteria for colorectal disorders: implications for clinical practice. *Curr Gastroenterol Rep*. 2017;19(4):15.
- Chedid V, Vijayvargiya P, Halawi H, et al. Audit of the diagnosis of rectal evacuation disorders in chronic constipation. *Neurogastroenterol Motil*. 2019;31(1):e13510.
- Vidlock EJ, Lembo A, Cremonini F. Diagnostic testing for dyssynergic defecation in chronic constipation: meta-analysis. *Neurogastroenterol Motil*. 2013;25(6):509–20.
- Dik VK, Siersema PD, Joseph A, et al. Constipation-related direct medical costs in 16 887 patients newly diagnosed with chronic constipation. *Eur J Gastroenterol Hepatol*. 2014;26(11):1260–6.
- Caetano AC, Santa-Cruz A, Rolanda C. Digital rectal examination and balloon expulsion test in the study of defecatory disorders: are they suitable as screening or excluding tests? *Can J Gastroenterol Hepatol*. 2016; ID 8654314.
- Altomare DF, Spazzafumo L, Rinaldi M, et al. Set-up and statistical validation of a new scoring system for obstructed defaecation syndrome. *Colorectal Dis*. 2008;10(1):84–8.
- Renzi A, Brillantino A, Di Sarno G, et al. Five-item score for obstructed defecation syndrome: study of validation. *Surg Innov*. 2013;20(2):119–25.
- Minguez M, Herrerros B, Sanchiz V, et al. Predictive value of the balloon expulsion test for excluding the diagnosis of pelvic floor dyssynergia in constipation. *Gastroenterology*. 2004;126(1):57–62.
- Noelting J, Ratuapli SK, Bharucha AE, et al. Normal values for high-resolution anorectal manometry in healthy women: effects of age and significance of rectoanal gradient. *Am J Gastroenterol*. 2012;107:1530–6.
- Chiarioni G, Kim SM, Vantini I, et al. Validation of the balloon evacuation test: reproducibility and agreement with findings from anorectal manometry and electromyography. *Clin Gastroenterol Hepatol*. 2014;12(12):2049–54.
- Talley NJ. How to do and interpret a rectal examination in gastroenterology. *Am J Gastroenterol*. 2008;103:820–2.
- Orkin BA, Sinykin SB, Lloyd PC. The digital rectal examination scoring system (DRESS). *Dis Colon Rectum*. 2010;53(12):1656–60.
- Bellini M, Usai-Satta P, Bove A, et al. Chronic constipation diagnosis and treatment evaluation: the “CHRO.CODI.T.E.” study. *BMC Gastroenterol*. 2017;17(1):11.
- Tantiphlachiva K, Rao P, Attaluri A, et al. Digital rectal examination is a useful tool for identifying patients with dyssynergia. *Clin Gastroenterol Hepatol*. 2010;8(11):955–60.
- Caetano AC, Dias S, Santa-Cruz A, et al. Renzi score for obstructed defecation syndrome—validation of the portuguese version according to the cosmin checklist. *Arq Gastroenterol*. 2018;55(1):55–60.
- Mokkink L, Terwee C, Patrick D. The COSMIN checklist manual. 2012: 1–56.
- Beaton DE, Bombardier C, Guillemin F, et al. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine (Phila Pa 1976)*. 2000;25(24):3186–91.
- Rao SSC, Mudipalli RS, Stessman M, et al. Investigation of the utility of colorectal function tests and Rome II criteria in dyssynergic defecation (Anismus). *Neurogastroenterol Motil*. 2004;16(5):589–96.
- Noelting J, Eaton JE, Choung RS, et al. The incidence rate and characteristics of clinically diagnosed defecatory disorders in the community. *Neurogastroenterol Motil*. 2016;28(11):1690–7.
- Ramage L, Georgiou P, Qiu S, et al. Can we correlate pelvic floor dysfunction severity on MR defecography with patient-reported symptom severity? *Updates Surg*. 2018;70(4):467–76.
- Eltringham MT, Khan U, Bain IM, et al. Functional defecation disorder as a clinical subgroup of chronic constipation: analysis of symptoms and physiological parameters. *Scand J Gastroenterol*. 2008;43(3):262–9.
- Ratuapli S, Bharucha AE, Harvey D, Zinsmeister AR. Comparison of rectal balloon expulsion test in seated and left lateral positions. *Neurogastroenterol Motil*. 2013;25(12):e813–20.

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PART III.

DISCUSSION AND CONCLUSIONS

CHAPTER 7. GENERAL DISCUSSION

7.1 Exploring Epidemiology – searching a meaning for what we found

CC is a worldwide prevalent condition with significant direct and indirect cost. CC and its subgroups are defined by the Rome IV criteria (Aziz et al. 2020) using both symptoms and objective physiological criteria that adds complexity and costs to this common condition.

When we started drawing the tasks, our main questions were “how can we understand better this condition in our own population? and are there ways to make the initial approach easier?”

First of all, we immediately identified a wide variation of the prevalence of CC, as well as discrepancies regarding its predictive or associated factors. (Werth et al 2019) We believed that epidemiology and influential aspects of CC in our community could shed some light and comprehension to the subject, turning our approach more efficient.

Our study sample included 1950 individuals and the rate of response was 68%. Our population presented a constipation rate of 17.8%, what goes in line with other European demographic studies. (Peppas et al. 2008) We considered quite remarkable that the prevalence of CC remains consistent using the Rome IV criteria, what strengthens its diagnostic value. Our survey is the first European population survey using the Rome IV criteria to define constipation in an adult epidemiological study. We also could discriminate the population prevalence of FC (9.3%) and IBS-C (8.5%) and this division allowed us to evaluate the association of certain specific features. We were not able to calculate the prevalence for DD in that population-based study sample as it was an out-of-hospital project.

Secondary aims were the identification of factors related to CC and health-seeking behaviours. Highlighting the differences to other studies, in our population, being solo and professionally not active were associated with constipation. This might be explained by less regularity of daily routines in these patients. Individuals of lower social, economic and educational level have a tendency towards higher constipation rates according to other authors (Peppas et al. 2008; Bytzer et al. 2001) but in our sample, only low-income was associated with CC. Our explanation for this difference is that maybe educational, social and economic level are not so closely related in the Portuguese population as in other study populations.

Unexpectedly there were no differences in terms of diet factors. MD was extensively studied in terms of cardiovascular benefit and overall survival, but regarding bowel habits, as far as we know only Agakidis *et al.* concluded that good adherence to the MD in a younger population was

associated to lower prevalence of functional gastrointestinal diseases. (Agakidis et al. 2019) Attending to our geographic location, our expectation was that the MD would be a positive influential factor of bowel and defecatory function in our study population, but we did not identify any association. But on the other hand, poor diet habits are usually associated with low income (Darmon & Drewnowski 2015) and that was an important demographic factor in our CC population. Maybe that aspect could overcome any beneficial influence of our Mediterranean position. Not surprisingly, physical inactivity was more frequent in constipated individuals as described by others (Tantawy et al. 2017) and this data adds evidence pointing to the continuous effort in terms of patient education regarding physical exercise.

We identified time at defecation of more than 5 minutes as a factor associated with constipation. That make us wondering if this feature is additionally important when we evaluate bowel habits. (Garg & Singh 2017) The "TONE" mnemonic habits (T, 3 minutes at defecation; O, once-a-day defecation frequency; N, no straining during passing motions; E, enough fibre) was associated with improvement in deranged defecation habits and haemorrhoidal disease according to Garg and Singh. Verkuil S *et al.* also identify "straining for more than five minutes" as one reliable indicator of chronic constipation. (Verkuil et al. 2020) We believe that time at defecation is probably an underestimated indicator, which is important to integrate in our clinical interview and to work it in our therapeutic plan with constipated patients.

This task also revealed some unexplored toilet behaviours and their association with constipation. Toilet behaviours associated with CC were the absence of morning evacuation habit, the use of triggers (such as coffee, cigarette, gym) and the use of reading or technological material to help the defecation process. The absence of the morning evacuation habit is probably explained by the pathophysiological mechanisms of constipation, making harder to control the time-scheduled bowel evacuation. Reading and technological material use is described by more than 60% of the constipated subjects in our study. This could be merely an echo of our times. But if we imagine these constipated patients spending more than 5 minutes at the toilet, maybe the use of reading or technological material could relax them, even if not helping specifically the defecation (at least not consciously). (Goldstein et al. 2009) When looking at the subanalysis, FC patients do not present an evacuation regularity, and this can explain the need for the more frequent use of triggers and squatting devices – the absence of an evacuation pattern pressures patients for a rigid toilet commitment to improve the bowel habits in FC, not so demanding with the more intermittent nature of IBS complains. This is the first study addressing toilet behaviour and its association with

bowel dysfunction. It would be interesting to see future studies of different socio-cultural populations reporting toilet habits.

Another aspect with insufficient data described is the healthcare related behaviours. Although they seek for a diversity of healthcare support, only 39% of constipated individuals seek for medical advice. The seek for pharmaceutical, alternative and psychological help was also associated with constipation as well as the use of laxatives (over-the-counter and prescribed). Maybe the proximity to the pharmacist, herbalist or shopkeeper and ease of access to laxatives (even the controls described its occasional use) can explain the growing seek of any form of help regarding bowel habits. At this point, there was also a significant difference between our FC and IBS-C patients - the concern and healthcare for bowel habits are reported more frequently by IBS-C individuals compared to FC individuals. This can be explained by the abdominal pain that characterizes IBS, a troublesome symptom that probably raises fears in these commonly anxious patients. (Hu et al. 2021)

Advantages of this study are its good size, its reliance on a sample of the general population, and the use of the most recent and standardized CC definition. The systematic sampling and age stratification to define our study population reduced selection bias. The main weakness of the study is the use of recall information and the sample size that could be even larger; by other hand, additional information could have been collected, for instance gynecological background in this predominant female population.

This was indeed a refreshing epidemiological study enlightening some aspects of constipated patients' behaviours.

7.2 Anorectal evaluation in the CC algorithm – where were we?

A pro-active cost-effective attitude in a highly prevalent condition as CC can be a real challenge. A creative method to screen constipated patients, particularly defecation disorders, was delineated. Our previously published meta-analysis calculated a pooled sensitivity and specificity for the BET of 67% and 80% respectively and a pooled sensitivity and specificity for the DRE of 80% and 84% respectively (Caetano et al. 2016).

But as stated before, BET was not standardized regarding the time, volume, position and material used in the technique. (Kassis et al. 2015; Chiarioni et al. 2014; Minguez et al. 2004; Glia et al. 1998) Chiarioni *et al.* addressed the issue of time of the BET and found a perfect reproducibility in 280 patients with constipation using a cut-off of 2 minutes, adding value to this attractive screening

option. (Chiarioni et al. 2014) One of the most significant aspects is the volume used in the BET. Minguéz *et al.* used a different physiological rationale regarding the BET (Minguéz et al. 2004) They used a variable volume associated with a permanent desire to evacuate to overcome rectal sensitivity bias and raised the BET value as an excluding tool (NPV of 98%). As far as we know, no study evaluated fixed and variable volumes on the testing protocol of the BET. A wide range of possible explanations for the moderate sensitivity and specificity of the BET compared to the “classic” physiological tests includes the phenotypic heterogeneity of DD (Cook et al. 2009; Bharucha et al. 2005), the lack of standardization between studies and the uncomfortable settings in which BET is performed. (Bharucha & Rao 2014)

Regarding the DRE, although guidelines highlight the importance of rectal examination for identifying DD (Bharucha et al. 2013), we only collected 4 studies evaluating the DRE. Maybe the reason is the emphasis given nowadays to technology rather than to clinical skills (Drossman 2004), making a simple tool like DRE underused. (Orkin et al. 2010)

In addition, no clinical score has emerged as a relevant diagnostic method in the evaluation flowchart of DD and none was ever evaluated as a screening tool.

That was our “starting point”.

7.3 Anorectal evaluation – where did we go further?

We selected 3 low-cost tools in order to understand their role in the screen of DD in constipated patients – a clinical score, the BET and the DRE - envisioning to overcome some of the lack of information and questions roused along the initial meta-analysis.

7.3.1 Clinical scores - Choice and validation process

Two specific DD clinical scores (Altomare score and Renzi score) were validated to grade severity and value of treatment's efficacy. (Renzi et al. 2013; Altomare et al. 2008) Two important limitations prevented us from using Altomare score – it includes “time spent at the toilet” and “stool consistency”, items with a potential cultural influence and diet effect. The Renzi score is a 5-items score (table 6) that assesses various complains of an abnormal evacuation and shows less cultural impact.

Since Renzi score was successfully validated in the English language, showing good discriminatory power to distinguish between patients and controls and changes in patients over time, we decided to validate a Portuguese version of Renzi score following COnsensus-based Standards for the

selection of health status Measurement Instruments (COSMIN) checklist guidelines. (COSMIN checklist manual 2012)

We were able to validate the domains of reliability, validity, responsiveness and interpretability (at group level) of Renzi score, following strict methodology based in the COSMIN checklist. Although the main goal of the work was achieved, there were some limitations - questionnaires applied at baseline were done by face-to-face interview and score application at 2 weeks and 3 months occurred by telephone; the 3 months' follow-up to evaluate clinical perceived change by patients is probably not enough, since this is a chronic disability which may not change much in such a short period of time.

Finally, our work validated the Portuguese version of Renzi score. We were then able to use this reliable, responsive, and interpretable tool to evaluate Portuguese constipated patients.

7.3.2 Value of optimization and combination of low-cost tools

This prospective study was conducted to assess the potential role of the selected low-cost tools in the evaluation of constipated individuals. Ninety-eight constipated patients were evaluated. Besides the gold standard physiological tests, constipated patients answered the clinical DD score and were evaluated by the DRE and the BET (standard and variable volume (w)). Demographic and clinical characteristics of both DD patients and NoDD patients were identical except for age as DD patients were significantly older (60 vs 51 years old) but that is also reported in other series and can be explained by the cumulative structural and physiological alterations in the pelvic floor of older patients. (Carrington et al. 2020; Chedid et al. 2019; Bharucha & Rao 2014; Bharucha et al. 2013; Noelting et al. 2013)

In our study population, the clinical score did not perform well as a screening tool (sensitivity 65% and specificity 10%). In fact, Renzi *et al.* validated their score specifically to grade defecation disorders and not as a diagnostic tool among constipated patients. Besides, their patients' sample was selected according to Rome III criteria and specific exclusion criteria – no irritable bowel syndrome and no slow transit constipation. Taking those aspects into account, it was not possible to reproduce their good results using the score as a screening tool. Besides, no item of the clinical DD score had a distinctive individualized performance.

Regarding the BET, in an attempt to discriminate the best performance of the BET, besides the standard BET, the wBET was also performed. The cut-off of 2 minutes was used as proposed by Chiaroni *et al.* (Charioni et al. 2014) The sequential BET - wBET followed by standard BET -

improved the BET performance in the evaluation of DD, with a sensitivity of 86%, specificity of 67%, PPV of 63% and NPV of 87%, revealing to be the most significant predictor for DD screening. These results points to the importance of rectal filling and its conscious awareness for a correct BET, improving the BET capability as a screening tool. Our data validate Minguéz *et al.* results. (Minguéz et al. 2004) Upgrading the technique, we add the rectal sensitivity in the wBET to the anorectal coordination in the standard BET – so patients able to expel both the balloons most probably do not have DD. We also share their enthusiasm that simple tools can be easily performed in any examination room and can be incorporated in the preliminary evaluation of constipated patients. The DRE score did not perform well as a screening tool. Compared with the results presented by Tantiphlachiva *et al.* in their sample of 209 patients (sensitivity of 75% and specificity of 87%), the DRE score had a poorer performance in our study population (sensitivity 29% and specificity 82%). (Tantiphlachiva et al. 2010) The DRE is an operator-dependent technique. Although we tried to decrease this bias with the execution of the DRE always by the same operator, we still have to take into account the years of professional experience of the main investigator (5 years) compared with the Tantiphlachiva team. It would be interesting to evaluate the learning curve of the DRE technique. Another possible bias is the cultural barrier – it is a dynamic evaluation and different populations may not consistently perform the same oral instructions.

This study had some limitations already pointed out – cultural barrier regarding the patients, years of experience regarding the investigators. The left lateral position to perform the BET can also be seen as a limitation as the sitting position is more physiological. (Ratuapli et al. 2013) The sample size can also be seen as a limitation. In our defense, while both the clinical score and the DRE score did not reveal discriminative power to screen constipated patients, the standard BET had a similar performance to that reported by other series. (Caetano et al. 2016) Besides, as we know, an algorithm or score always performs better in the validation population (reported in the original papers) and the consistency of the results when performing the external validation is often not achieved.

Emerging from the apparently less valuable clinical scores and DRE, the sequential BET stood up as an attractive screening tool for DD in this prospective study. The sequential BET could become an interesting tool for screening constipated patients in the Primary Care setting.

CHAPTER 8. MAINS CONCLUSIONS

We performed the first epidemiological study regarding CC in an adult population of an European Mediterranean country using Rome IV Criteria. As far as we know, it is also the first time that an exhausting evaluation of associated factors, toilet behaviours and healthcare seeking is achieved, helping us to understand better the constipated individuals. Using Rome IV criteria, CC seems to impact 1 in each 5 European Mediterranean individuals. In our study population, constipated patients are younger, solo, less active and with low income. Curiously and not described before, constipated individuals develop a clear toilet behaviour profile. The toilet behaviours seem more complex in FC, inversely the healthcare seeking behaviour seems more frequent in IBS-C.

Low-cost tools in the evaluation of constipated patients could be an attractive and simple methodology to identify DD that warrant a specific approach. With this in mind, we performed a prospective study, in a constipated population, applying a validated clinical score, the DRE and the standard and wBET, in an individualized and combined algorithmic evaluation. The clinical DD score and the DRE did not reveal discriminative power to evaluate patients with DD. The BET stands as a good, reproducible and low-cost tool with a high NPV for DD, that performs better when sequentially used with variable volume and fixed volume. So, pursuing the refinement of the low-cost tools, the sequential BET seems the most suitable screening tool with potential use in the Primary Care setting. That way, constipated individuals with a normal sequential BET are less likely to have a DD and to proceed to a complicated diagnostic algorithm in a tertiary center.

CHAPTER 9. NEW PERSPECTIVES

Getting this far, it always seems an incomplete work. Still, many questions remain unanswered.

One future aim is to further assess the sequential BET value in a first approach of constipated individuals in the Primary Care setting.

One other unexplored area is the interventional nonmedical approach of the toilet habits of constipated individuals.

An evaluation of the direct and indirect costs regarding CC diagnosis and management in a European country is another important task not previously performed.

One other aspect not fully explored is the discrepancy between patients' and healthcare providers' perceptions of constipation symptoms and the impact of symptoms in patients' life.

New challenges in each corner of the way make the sightseeing more beautiful.

PART IV.

BIBLIOGRAPHY

- Agakidis, C., Kotzakioulafi, E., Petridis, D., Apostolidou, K., & Karagiozoglou-Lampoudi, T. (2019). Mediterranean Diet Adherence is Associated with Lower Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents. *Nutrients*, *11*(6), 1283.
- Altomare, D. F., Spazzafumo, L., Rinaldi, M., Dodi, G., Ghiselli, R., & Piloni, V. (2008). Set-up and statistical validation of a new scoring system for obstructed defaecation syndrome. *Colorectal disease: the official journal of the Association of Coloproctology of Great Britain and Ireland*, *10*(1), 84–88.
- Aziz, I., Whitehead, W. E., Palsson, O. S., Törnblom, H., & Simrén, M.. (2020). An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. *Expert review of gastroenterology & hepatology*, *14*(1), 39–46.
- Bharucha, A. E., Fletcher, J. G., Seide, B., Riederer, S. J., & Zinsmeister, A. R. (2005). Phenotypic variation in functional disorders of defecation. *Gastroenterology*, *128*(5), 1199–1210.
- Bharucha, A. E., & Lacy, B. E. (2020). Mechanisms, Evaluation, and Management of Chronic Constipation. *Gastroenterology*, *158*(5), 1232–1249.e3.
- Bharucha, A. E., & Wald, A. (2019). Chronic Constipation. *Mayo Clinic proceedings*, *94* (11), 2340–2357.
- Bharucha, A. E., Pemberton, J. H., & Locke, G. R., 3rd (2013). American Gastroenterological Association technical review on constipation. *Gastroenterology*, *144*(1), 218–238.
- Bharucha, A.E., & Rao, S. S. (2014). An update on anorectal disorders for gastroenterologists. *Gastroenterology*, *146*(1), 37–45.e2.
- Bordeianou, L., Savitt, L., & Dursun, A. (2011). Measurements of pelvic floor dyssynergia: which test result matters?. *Diseases of the colon and rectum*, *54*(1), 60–65.
- Bytzer, P., Howell, S., Leemon, M., Young, L. J., Jones, M. P., & Talley, N. J. (2001). Low socioeconomic class is a risk factor for upper and lower gastrointestinal symptoms: a population-based study in 15 000 Australian adults. *Gut*, *49*(1), 66–72.
- Caetano, A. C., Santa-Cruz, A., & Rolanda, C. (2016). Digital Rectal Examination and Balloon Expulsion Test in the Study of Defecatory Disorders: Are They Suitable as Screening or Excluding Tests?. *Canadian journal of gastroenterology & hepatology*, *2016*, 8654314.

- Carrington, E. V., Heinrich, H., Knowles, C. H., Fox, M., Rao, S., Altomare, D. F., Bharucha, A. E., Burgell, R., Chey, W. D., Chiarioni, G., Dinning, P., Emmanuel, A., Farouk, R., Felt-Bersma, R., Jung, K. W., Lembo, A., Malcolm, A., Mittal, R. K., Mion, F., Myung, S. J., ... All members of the International Anorectal Physiology Working Group (2020). The international anorectal physiology working group (IAPWG) recommendations: Standardized testing protocol and the London classification for disorders of anorectal function. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, 32(1), e13679.
- Chedid, V., Vijayvargiya, P., Halawi, H., Park, S. Y., & Camilleri, M. (2019). Audit of the diagnosis of rectal evacuation disorders in chronic constipation. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, 31(1), e13510.
- Chiarioni, G., Kim, S. M., Vantini, I., & Whitehead, W. E. (2014). Validation of the balloon evacuation test: reproducibility and agreement with findings from anorectal manometry and electromyography. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, 12(12), 2049–2054.
- Chiarioni, G., Salandini, L., & Whitehead, W. E. (2005). Biofeedback benefits only patients with outlet dysfunction, not patients with isolated slow transit constipation. *Gastroenterology*, 129(1), 86–97.
- Cook, I. J., Talley, N. J., Benninga, M. A., Rao, S. S., & Scott, S. M. (2009). Chronic constipation: overview and challenges. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, 21 Suppl 2, 1–8.
- Darmon, N., & Drewnowski, A. (2015). Contribution of food prices and diet cost to socioeconomic disparities in diet quality and health: a systematic review and analysis. *Nutrition reviews*, 73(10), 643–660.
- Dik, V. K., Siersema, P. D., Joseph, A., Hodgkins, P., Smeets, H. M., & van Oijen, M. G. (2014). Constipation-related direct medical costs in 16 887 patients newly diagnosed with chronic constipation. *European journal of gastroenterology & hepatology*, 26(11), 1260–1266.
- Drossman D. A. (2016). Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. *Gastroenterology*, S0016-5085(16)00223-7.
- Drossman D. A. (2004). Medicine has become a business, but what is the cost?. *Gastroenterology*, 126(4), 952–953.

- Eltringham, M. T., Khan, U., Bain, I. M., Wooff, D. A., Mackie, A., Jefferson, E., & Yiannakou, Y. (2008). Functional defecation disorder as a clinical subgroup of chronic constipation: analysis of symptoms and physiological parameters. *Scandinavian journal of gastroenterology*, *43*(3), 262–269.
- Gálvez, C., Garrigues, V., Ortiz, V., Ponce, M., Nos, P., & Ponce, J. (2006). Healthcare seeking for constipation: a population-based survey in the Mediterranean area of Spain. *Alimentary pharmacology & therapeutics*, *24*(2), 421–428.
- Garg, P., & Singh, P. (2017). Adequate dietary fiber supplement and TONE can help avoid surgery in most patients with advanced hemorrhoids. *Minerva gastroenterologica e dietologica*, *63*(2), 92–96.
- Gladman, M. A., Lunniss, P. J., Scott, S. M., & Swash, M. (2006). Rectal hyposensitivity. *The American journal of gastroenterology*, *101*(5), 1140–1151.
- Glia, A., Lindberg, G., Nilsson, L. H., Mihocsa, L., & Akerlund, J. E. (1998). Constipation assessed on the basis of colorectal physiology. *Scandinavian journal of gastroenterology*, *33*(12), 1273–1279.
- Goldstein, O., Shaham, Y., Naftali, T., Konikoff, F., Lavy, A., & Shaoul, R. (2009). Toilet reading habits in Israeli adults. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, *21*(3), 291–295.
- Halverson, A. L., & Orkin, B. A. (1998). Which physiologic tests are useful in patients with constipation?. *Diseases of the colon and rectum*, *41*(6), 735–739.
- Higgins, P. D., & Johanson, J. F. (2004). Epidemiology of constipation in North America: a systematic review. *The American journal of gastroenterology*, *99*(4), 750–759.
- Hu, Z., Li, M., Yao, L., Wang, Y., Wang, E., Yuan, J., Wang, F., Yang, K., Bian, Z., & Zhong, L. (2021). The level and prevalence of depression and anxiety among patients with different subtypes of irritable bowel syndrome: a network meta-analysis. *BMC gastroenterology*, *21*(1), 23.
- Jones, P. N., Lubowski, D. Z., Swash, M., & Henry, M. M. (1987). Is paradoxical contraction of puborectalis muscle of functional importance?. *Diseases of the colon and rectum*, *30*(9), 667–670.
- Jones, R., & Ballard, K. (2008). Healthcare seeking in gastro-oesophageal reflux disease: a qualitative study. *European journal of gastroenterology & hepatology*, *20*(4), 269–275.

- Kanmaniraja, D., Arif-Tiwari, H., Palmer, S. L., Kamath, A., Lewis, S. C., Flusberg, M., Kobi, M., Lockhart, M. E., & Chernyak, V. (2021). MR defecography review. *Abdominal radiology (New York)*, *46*(4), 1334–1350.
- Kassis, N. C., Wo, J. M., James-Stevenson, T. N., Maglinte, D. D., Heit, M. H., & Hale, D. S. (2015). Balloon expulsion testing for the diagnosis of dyssynergic defecation in women with chronic constipation. *International urogynecology journal*, *26*(9), 1385–1390.
- Mibu, R., Hotokezaka, M., Kai, T., Tanabe, Y., & Tanaka, M. (2001). A simplified defaecographic procedure for the assessment of faecal incontinence or obstructed defaecation. *Colorectal disease: the official journal of the Association of Coloproctology of Great Britain and Ireland*, *3*(5), 328–333.
- Minguez, M., Herreros, B., Sanchiz, V., Hernandez, V., Almela, P., Añon, R., Mora, F., & Benages, A. (2004). Predictive value of the balloon expulsion test for excluding the diagnosis of pelvic floor dyssynergia in constipation. *Gastroenterology*, *126*(1), 57–62.
- Mokkink L, Terwee C, Patrick D. The COSMIN checklist manual. 2012: 1–56.
- Mugie, S. M., Benninga, M. A., & Di Lorenzo, C. (2011). Epidemiology of constipation in children and adults: a systematic review. *Best practice & research. Clinical gastroenterology*, *25*(1), 3–18.
- Murad-Regadas, S. M., Regadas, F. S., Rodrigues, L. V., Silva, F. R., Soares, F. A., & Escalante, R. D. (2008). A novel three-dimensional dynamic anorectal ultrasonography technique (echodefecography) to assess obstructed defecation, a comparison with defecography. *Surgical endoscopy*, *22*(4), 974–979.
- Noelting, J., Eaton, J. E., Choung, R. S., Zinsmeister, A. R., Locke, G. R., 3rd, & Bharucha, A. E. (2016). The incidence rate and characteristics of clinically diagnosed defecatory disorders in the community. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, *28*(11), 1690–1697.
- Noelting, J., Ratuapli, S. K., Bharucha, A. E., Harvey, D. M., Ravi, K., & Zinsmeister, A. R. (2012). Normal values for high-resolution anorectal manometry in healthy women: effects of age and significance of rectoanal gradient. *The American journal of gastroenterology*, *107*(10), 1530–1536.
- Orkin, B. A., Sinykin, S. B., & Lloyd, P. C. (2010). The digital rectal examination scoring system (DRESS). *Diseases of the colon and rectum*, *53*(12), 1656–1660.
- Peppas, G., Alexiou, V. G., Mourtzoukou, E., & Falagas, M. E. (2008). Epidemiology of constipation in Europe and Oceania: a systematic review. *BMC gastroenterology*, *8*, 5.

- Preston, D. M., & Lennard-Jones, J. E. (1985). Anismus in chronic constipation. *Digestive diseases and sciences*, *30*(5), 413–418.
- Rao, S. S., Hatfield, R., Soffer, E., Rao, S., Beaty, J., & Conklin, J. L. (1999). Manometric tests of anorectal function in healthy adults. *The American journal of gastroenterology*, *94*(3), 773–783.
- Rao, S. S., Kavlock, R., & Rao, S. (2006). Influence of body position and stool characteristics on defecation in humans. *The American journal of gastroenterology*, *101*(12), 2790–2796.
- Rao, S. S., Mudipalli, R. S., Stessman, M., & Zimmerman, B. (2004). Investigation of the utility of colorectal function tests and Rome II criteria in dyssynergic defecation (Anismus). *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, *16*(5), 589–596.
- Rao, S. S., Welcher, K. D., & Leistikow, J. S. (1998). Obstructive defecation: a failure of rectoanal coordination. *The American journal of gastroenterology*, *93*(7), 1042–1050.
- Ratuapli, S., Bharucha, A. E., Harvey, D., & Zinsmeister, A. R. (2013). Comparison of rectal balloon expulsion test in seated and left lateral positions. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, *25*(12), e813–e820.
- Ratuapli, S. K., Bharucha, A. E., Noelting, J., Harvey, D. M., & Zinsmeister, A. R. (2013). Phenotypic identification and classification of functional defecatory disorders using high-resolution anorectal manometry. *Gastroenterology*, *144*(2), 314–322.e2.
- Raza, N., & Bielefeldt, K. (2009). Discriminative value of anorectal manometry in clinical practice. *Digestive diseases and sciences*, *54*(11), 2503–2511.
- Renzi, A., Brillantino, A., Di Sarno, G., & d'Aniello, F. (2013). Five-item score for obstructed defecation syndrome: study of validation. *Surgical innovation*, *20*(2), 119–125.
- Sakakibara, R., Tsunoyama, K., Hosoi, H., Takahashi, O., Sugiyama, M., Kishi, M., Ogawa, E., Terada, H., Uchiyama, T., & Yamanishi, T. (2010). Influence of Body Position on Defecation in Humans. *Lower urinary tract symptoms*, *2*(1), 16–21.
- Schmulson, M. J., & Drossman, D. A. (2017). What Is New in Rome IV. *Journal of neurogastroenterology and motility*, *23*(2), 151–163.
- Simren, M., Palsson, O. S., & Whitehead, W. E. (2017). Update on Rome IV Criteria for Colorectal Disorders: Implications for Clinical Practice. *Current gastroenterology reports*, *19*(4), 15.

- Siproudhis, L., Pigot, F., Godeberge, P., Damon, H., Soudan, D., & Bigard, M. A. (2006). Defecation disorders: a French population survey. *Diseases of the colon and rectum*, 49(2), 219–227.
- Suares, N. C., & Ford, A. C. (2011). Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. *The American journal of gastroenterology*, 106(9), 1582–1592.
- Talley N. J. (2008). How to do and interpret a rectal examination in gastroenterology. *The American journal of gastroenterology*, 103(4), 820–822.
- Tantawy, S. A., Kamel, D. M., Abdelbasset, W. K., & Elgohary, H. M. (2017). Effects of a proposed physical activity and diet control to manage constipation in middle-aged obese women. *Diabetes, metabolic syndrome and obesity: targets and therapy*, 10, 513–519.
- Tantiplachiva, K., Rao, P., Attaluri, A., & Rao, S. S. (2010). Digital rectal examination is a useful tool for identifying patients with dyssynergia. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, 8(11), 955–960.
- Verkuijl, S. J., Meinds, R. J., Trzpis, M., & Broens, P. (2020). The influence of demographic characteristics on constipation symptoms: a detailed overview. *BMC gastroenterology*, 20(1), 168.
- Vidlock, E. J., Lembo, A., & Cremonini, F. (2013). Diagnostic testing for dyssynergic defecation in chronic constipation: meta-analysis. *Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society*, 25(6), 509–520.
- Voderholzer, W. A., Neuhaus, D. A., Klauser, A. G., Tzavella, K., Müller-Lissner, S. A., & Schindlbeck, N. E. (1997). Paradoxical sphincter contraction is rarely indicative of anismus. *Gut*, 41(2), 258–262.
- Werth, B. L., Williams, K. A., Fisher, M. J., & Pont, L. G. (2019). Defining constipation to estimate its prevalence in the community: results from a national survey. *BMC gastroenterology*, 19(1), 75.