see related editorial on page 885

Chronic Constipation, Irritable Bowel Syndrome With Constipation and Constipation With Pain/Discomfort: Similarities and Differences

Enrique Rey, MD, PhD¹, Agustín Balboa, MD² and Fermín Mearin, MD, PhD²

- OBJECTIVES: Some patients with chronic constipation (CC) have abdominal pain and discomfort (painful CC) without fulfilling the criteria for irritable bowel syndrome (IBS). Our aim was to investigate similarities and differences among nonpainful CC, painful CC, and CC in patients with IBS according to prevalence, individual symptoms, associated factors, and impact on health-related quality of life and use of medical resources.
- METHODS: We conducted a telephone survey of a random sample of the Spanish population (*N*=1500). Bowel symptoms were recorded using the Rome III questionnaire, health-related quality of life using the short form-12 (SF-12) and quality of live in constipation-20 (CVE-20) questionnaires, and self-reported constipation, lifestyle habits, and consultation behavior using an *ad hoc* questionnaire.
- RESULTS: The overall prevalence of CC was 19.2%, with prevalence by subgroups being 13.9% for nonpainful CC, 2.0% for painful CC, and 3.3% for CC in patients with IBS. CC was more prevalent among women at a ratio of 2.7:1. Subjects with painful CC and CC in patients with IBS were younger, reported more constipation, and had more symptoms than subjects with nonpainful CC. Age and physical activity were significantly associated with CC. Symptoms associated with consultation were abdominal pain and digitation. Nonpainful CC patients were more satisfied with laxative use than were the other subgroups. Subjects with CC showed a significant impairment in the physical and mental component of the SF-12 questionnaire.
- CONCLUSIONS: CC appears to be a spectrum; most patients do not have abdominal pain/discomfort but others (with otherwise quite similar characteristics) are patients with IBS or are out of any established diagnosis.

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

Am J Gastroenterol 2014; 109:876-884; doi:10.1038/ajg.2014.18; published online 4 March 2014

INTRODUCTION

Chronic constipation (CC) and irritable bowel syndrome (IBS) are two very frequent conditions. CC prevalence among the general population in western countries ranges from 2 to 24% (1–3), and is about 40% in subjects aged older than 65 years (4). IBS prevalence ranges from 3 to 14% (5,6). For both conditions, prevalence figures depend very much on the criteria selected to make the diagnosis. Hence, pooled prevalence of CC varies from 15% when self-reported to 6.8% when diagnosed according to Rome III criteria (7). Similarly, IBS prevalence varies from 12% to 3% or 11% when using Rome I, Rome II, or Rome III criteria, respectively (8,9). In a previous study investigating constipation prevalence in Spain, the respective figures were 29% when self-reported vs. 19 and 14% when based on Rome I and Rome II criteria (10).

According to Rome III criteria, IBS patients are grouped into different subtypes based on the predominant stool consistency, i.e., IBS with constipation (IBS-C), IBS with diarrhea, mixedtype IBS, and unsubtyped IBS (11). By definition, all IBS subjects, including IBS-C patients, need to present with abdominal pain or discomfort to make the diagnosis, whereas in the case of CC, abdominal pain/discomfort are symptoms not included in the definition (11). Discriminating between these two disorders is

¹Department of Digestive Diseases, San Carlos Clinical Hospital, Complutense University, San Carlos Clinical Hospital Health Research Institute (Instituto de Investigacion Sanitaria del Hospital Clinico San Carlos (IdISSC)), Madrid, Spain; ²Service of Gastroenterology, Centro Médico Teknon, Institute of Functional and Motor Digestive Disorders, Barcelona, Spain. **Correspondence:** Fermín Mearin, MD, PhD, Service of Gastroenterology, Centro Médico Teknon, Institute of Functional and Motor Digestive Disorders, C/Vilana 12, E-08022 Barcelona, Spain. E-mail: mearin@dr.teknon.es **Received 26 April 2013; accepted 16 December 2013** not always easy; however, both share symptoms such as bloating (difficult to differentiate from discomfort), IBS-C patients may complain of only mild pain/discomfort, and CC patients sometimes have "some" pain/discomfort. Moreover, the same treatments (including new laxatives and prokinetics) have been used for both conditions with successful results (12–18). Indeed, there is a group of patients with constipation who experience abdominal pain/discomfort (painful CC), yet do not fulfill the criteria for precise diagnosis of IBS (19).

Some studies, using cluster analysis, have concluded that CC and IBS are two different disorders with different diagnostic criteria (11). In contrast, other researchers are of the opinion that both are part of a spectrum with constipation as the main symptom and abdominal pain as a variable symptom of the same disease (20).

Accordingly, our aim was to investigate similarities and differences among nonpainful CC, painful CC, and CC in patients with IBS in the general population, according to the following: (1) prevalence; (2) individual symptoms; (3) associated factors; and (4) impact on health-related quality of life and use of medical resources.

METHODS

Study population and survey method

A random sample of the Spanish population of both sexes aged 18 years or over was obtained from the national telephone directory in computerized format. This sample was stratified by sex, age, province, and size of town of residence in proportion to the number of inhabitants recorded for each Spanish population stratum by the 2009 National Population Census. The study was formally approved by the Clinical Research Ethics Committee of the Hospital Clinico San Carlos in Madrid, Spain. Sample size was set at 1,500 subjects, which allowed for estimation of a CC prevalence of 15% with 5% accuracy.

Telephone calls were made in the morning, afternoon, evening, and at night for 6 days a week, excluding Sundays, on the second fortnight of June 2011. Telephone numbers not corresponding to private dwellings were ruled out. Once telephone contact had been made with any given home, the scientific nature of the study was explained but without specifically mentioning constipation as an objective (so as not to bias participation and answers), and respondents were asked to give their formal consent to participating. In those cases where consent was forthcoming, respondents were questioned as to their age and sex, and, provided that they corresponded to the established stratum, the interview then proceeded. Where respondents failed to correspond to the stratum, we asked about any other resident who might possibly meet such criteria. Only one interview was conducted per home.

Data were collected by professional interviewers who had been trained by researchers in the study goals and methods, and in the features of the questionnaire. Information obtained by telephone interview was directly fed into the computer database by the interviewer. Interviews as well as data collection and data entry were constantly supervised by a professional with experience in this area.

Questionnaires

The following questionnaires were used to collect information directly from the subjects. Data on constipation-related and other digestive symptoms were collected using the validated Spanish version of the Rome III questionnaire (21).

Sociodemographic and general data were collected using the corresponding items of a validated questionnaire for telephone interview use in the Spanish population (22). General quality of life was measured with the short form-12 (SF-12) questionnaire (23).

We also collected information on some lifestyle habits (liquid intake, fiber intake, and physical exercise) with an ad hoc questionnaire. All persons were asked to average the number of glasses or cups of liquid (including water, refreshments, soup, and so on) that they were in the habit of drinking daily, during the course of the morning, lunch, evening, dinner, and night. Daily liquid intake was calculated as the sum of these amounts. Fiber intake was calculated with a simplified food frequency questionnaire (24), including six questions referring to the usual weekly intake of fruits (one question), vegetables (two questions), cereals (one question), legumes (one question), and nuts (one question). Answers were categorized as less than one ration weekly, one to three rations weekly, three to six rations weekly, one ration daily, and two or more rations daily; for calculations purposes, these categories were then summarized as 0.5, 2, 4.5, 7, and 14 rations weekly, respectively. Total fiber intake was calculated by assuming 2.5 g per ration of fruits, 3.5 g for vegetables, 1 g for cereals, 3g for legumes, and 1.5g for nuts, and was expressed as grams daily. To estimate physical activity, subjects were asked to describe their usual physical activity under one of the following heads: "do sports regularly"; "used to walking long distances"; "used to walking short distances (around my home)", or "not used to walking or just used to walking a little bit".

Subjects were asked whether they considered themselves as constipated and whether they have used laxatives in the preceding year. Using an *ad hoc* questionnaire, modified from a questionnaire previously used successfully in a population-based IBS survey (25), those who had answered affirmatively to at least one of the above questions were then asked whether they had sought constipation-related advice from a health professional in the preceding year, and what procedures, if any, they had undergone because of constipation. A constipation-specific quality of life questionnaire (quality of live in constipation-20, CVE-20) (26) was used on these subjects.

Definitions and variables of interest

We defined CC and IBS according to Rome III, applying the Rome III diagnostic algorithms (21). The specific question used to categorize individuals into nonpainful CC or painful CC was as follows: "In the last 3 months, how often have you had pain or discomfort in your abdomen?" Seven different possible answers were provided, namely, never, less than 1 day a month, 1 day a month, 2–3 days a month, 1 day a week, more than 1 day a week, or, every day. Individuals with nonpainful constipation were classified as such if they referred no pain or pain less than 2 days monthly over the previous 3 months.

	Total (N=1500) n (% (95% CI))	Females (N=762) n (% (95% CI))	Males (N=738) n (% (95% CI))
Age (years)			
18–40 (<i>N</i> =648)	121 (19 (15.7–21.7))	95 (30 (24.6–34.6))	26 (8 (5.0–10.9))
41–65 (<i>N</i> =653)	127 (19 (16.4–22.5))	87 (27 (21.8–31.4))	40 (12 (8.7–15.8))
>65 (<i>N</i> =199)	40 (20 (14.5–25.7))	28 (25 (16.7–32.5))	12 (14 (6.7–21.5))
BMI			
Normal (<25 kgm ⁻²) (<i>N</i> =772)	168 (22 (18.9–24.7))	132 (28 (24.3–32.6))	36 (12 (8.1–15.3))
Overweight (25–29.9 kg m ⁻²) (<i>N</i> =534)	81 (15 (12.1–18.2))	50 (25 (19.4–31.6))	31 (9 (6.1–12.3))
Obesity (30 kgm^{-2} or more) (<i>N</i> =192)	38 (20 (14.2–25.4))	27 (27 (18.1–35.4))	11 (12 (5.4–18.8))
Marital status			
Married (<i>N</i> =914)	182 (20 (17.3–22.5))	135 (29 (24.7–33.0))	47 (10 (7.7–13.4))
Single (<i>N</i> =405)	66 (16 (12.7–19.9))	46 (27 (20.0–33.2))	20 (9 (5.0–12.2))
Others (<i>N</i> =181)	40 (22 (16.1–28.1))	29 (24 (16.4–31.6))	11 (18 (8.5–28.1))
Educative level			
Primary (<i>N</i> =514)	99 (19 (15.9–22.7))	71 (24 (19.4–29.2))	28 (13 (8.2–17.0))
Secondary (N=554)	102 (18 (15.2–21.6))	76 (31 (24.9–36.4))	26 (8 (5.4–11.6))
University (<i>N</i> =432)	87 (20 (16.4–23.9))	63 (28 (22.4–34.3))	24 (11 (7.1–15.7))
Geographical area			
Mediterranean (N=815)	175 (21 (18.7–24.3))	127 (31 (26.6–35.5))	48 (12 (8.7–15.0))
Center (<i>N</i> =463)	80 (17 (13.8–20.7))	57 (24 (18.8–29.7))	23 (10 (6.2–14.0))
Atlantic (N=222)	33 (15 (10.2–19.5))	26 (22 (14.6–29.5))	7 (7 (1.9–11.6))
Habitat			
Rural (<i>N</i> =324)	57 (18 (13.4–21.7))	41 (24 (17.4–30.0))	16 (11 (5.7–15.5))
Urban (<i>N</i> =1176)	231 (20 (17.4–21.9))	169 (29 (25.0–32.3))	62 (11 (8.1–13.0))
Total	288 (19.2 (17.2–21.2))	210 (27.6 (24.4–30.7))	78 (9.1 (8.4–12.8))
CI, confidence interval.			

Table 1. Prevalence of chronic constipation according to demographic factors, stratified by gender

CC patients were classified into the following three different groups to single out any possible overlap between CC and IBS:

- Nonpainful CC: subjects with CC according to Rome III, not reporting abdominal pain or discomfort (or reporting such pain or discomfort less than 2–3 days per month over the previous 3 months).
- Painful CC: subjects with CC according to Rome III, reporting abdominal pain or discomfort at least
 2–3 days per month but not meeting criteria for IBS.
- (iii) CC in patients with IBS: subjects meeting criteria for both CC and IBS.

Nonconstipated subjects served as the control group.

All variables were modeled categorically using dummy terms. Categories of the variables can be seen in the Results section (**Table 1**). Body mass index (weight in kilograms divided by the square of height in meters) was modeled in three categories (normal <25, overweight 25–29.9, and obesity \geq 30 kg m⁻²); geographical area of residence was grouped into three areas, namely, Mediterranean (regions bordering on the Mediterranean Sea),

Central (landlocked regions), and Atlantic (regions bordering on the Atlantic Ocean). The Canary Islands were included in the Mediterranean area, as the habits and customs in the former are comparable to those in the latter. Rural or urban habitat was defined by the size of town of residence (under 30,000 inhabitants vs. 30,000 inhabitants and over). Fiber and liquid intake were estimated from subjects' answers and calculated as described above; for statistical analysis purposes, they were stratified by their respective quintiles. The SF-12 physical and mental components were calculated using the standard correction rules.

Statistical analysis

Prevalence of CC was accompanied by its 95% confidence interval (CI). We performed a descriptive analysis of constipation-related visits to doctors' offices, emergency rooms, hospitalization, and procedures.

The association between constipation and its potential risk factors was summarized by odds ratios (ORs) obtained from multiple logistic regressions, which, as independent variables, included sociodemographic variables, body mass index, total liquid intake, fiber intake, and physical exercise.

All statistical analyses were performed using the SPSS computer software package (SPSS Inc., Chicago, IL).

RESULTS

Response rate

A total of 10,184 telephone calls were made, 2,509 of which corresponded to private dwellings inhabited by Spanish-speaking subjects within the pre-established age, sex, provincial, and sizeof-town strata. Of these 2,509 subjects, 822 refused to participate in the interview, 1,500 provided valid interviews at the time of telephone contact, and 187 agreed to be interviewed at a subsequent



Figure 1. Clinical spectrum of chronic constipation. Note that some patients with CC also have criteria for IBS (IBS with constipation). CC, patients with symptoms of chronic constipation; IBS, irritable bowel syndrome.

 Table 2. Clinical spectrum of constipation

date, although these interviews never took place because the requisite target figure was attained before the envisaged appointment date. Thus, the survey response rate was 67.4%.

Prevalence of CC

Of the 555 (37%) interviewees who reported two or more defining symptoms of constipation according to Rome III, 317 (57%) reported having these symptoms for 6 months or longer. In this latter group, 288 subjects (91%) reported having loose stools never or occasionally; of these, 49 (17%) met criteria for IBS (23 subclassified as IBS-C and 26 as unsubtyped IBS). The prevalence of CC was thus 19.2% (95% CI: 17.2–21.2%).

Prevalence of CC according to demographic factors (age, body mass index, marital status, educative level, Spanish geographical area, and habitat), stratified by gender, is shown in **Table 1**.

The spectrum of CC

A breakdown of the 288 subjects showed that 209 met the definition of nonpainful CC, 30 the definition of painful CC, and 49 the criteria for CC with IBS. Hence, prevalence was 13.9% (95% CI: 12.2–15.7%) for nonpainful CC, 2.0% (95% CI: 1.3–2.7%) for painful CC, and 3.3% (95% CI: 2.4–4.2%) for CC in patients with IBS (**Figure 1**). Subjects with painful CC or CC with IBS were younger, reported more constipation, and had more constipation symptoms than subjects with nonpainful CC (**Table 2** and **Figure 2**).

Among nonpainful CC, painful CC, and CC in patients with IBS, no statistically significant differences were observed in terms of body mass index, marital status, educative level, Spanish

	Nonpainful CC (N=209)	Painful CC (N=30)	CC in patients with IBS (N=49)	Р
Prevalence	13.9% (12.2–15.7%)	2.0% (1.3–2.7%)	3.3% (2.4–4.2%)	
Age (years) (X (s.d.))	47.4 (17.1)	40.3 (12.2)	42.1 (15.7)	0.02
Females (n (%))	145 (69)	27 (90)	38 (78)	0.04
Self-reported CC (n (%))	131 (63)	21 (70)	37 (75)	0.04
Laxatives use (n (%))	64 (31)	15 (50)	33 (67)	0.1
Consultation (n (%))	63 (30)	15 (50)	22 (45)	0.03
CC Symptoms				
Number of CC symptoms (X (s.d.))	3.2±1.2	3.7±1.4	3.6±1.5	0.06
Less than three BM weekly (n (%))	53 (25)	13 (43)	17 (35)	0.08
Hard stools (n (%))	79 (38)	18 (60)	23 (47)	0.05
Straining (n (%))	74 (35)	14 (47)	18 (37)	0.5
Incomplete evacuation (n (%))	194 (93)	30 (100)	45 (92)	0.3
Anal blockage (n (%))	190 (91)	27 (90)	42 (86)	0.5
Digitation (n (%))	84 (40)	10 (33)	29 (59)	0.03
SF12 (physical component) (X (s.d.))	48.5 (10.4)	47.7 (11.1)	46.1 (10.7)	0.5

BM, bowel movements; CC, chronic constipation; IBS, irritable bowel syndrome.



Figure 2. Bowel symptoms in patients with CC. CC, chronic constipation; IBS, irritable bowel syndrome.

geographical area, or habitat. Similarly, there were no differences in liquid intake, fiber intake, or physical exercise (**Table 3**).

Factors associated with CC

CC was statistically significantly more prevalent in women (27.6% (95% CI: 24.4–30.7%)) than in men (10.6% (95% CI: 8.4–12.8%)), i.e., a 2.7:1 ratio. CC displayed a slight trend toward increasing with age in the overall population, mainly owing to an increase with age among men. Among the sociodemographic factors (**Table 1**), geographical area of residence was associated with CC, regardless of gender, with the highest prevalence in the Mediterranean area (21.5% (95% CI: 8.7–24.3%)), the lowest prevalence in the Atlantic area (14.9% (95% CI: 10.2–19.5%)), and an intermediate prevalence in the central area (17.3% (95% CI: 13.8–20.7%)).

Among the lifestyle habits, prevalence of CC was inversely related to liquid intake and physical activity (P<0.01; χ^2 -test), in both men and women, and displayed a U-shaped prevalence curve in relation to fiber intake, as detailed in **Supplemental Table S1** online.

In the multivariate model analysis, only female gender (OR = 3.04 (2.28–4.05)) and physical activity ("do sports regularly" as reference category; "long walks": OR = 0.97 (0.66-1.43), "short walks": OR = 1.52 (1.06-2.19); "not used to walking": OR = 2.04 (1.23-3.39)) were independently associated with CC. When the analysis was performed separately in women and men, physical activity was linked to CC solely in women.

Burden of constipation in the community

Consultation. Of the 360 subjects who defined themselves as constipated or reported using laxatives in the preceding year, 143 (39.4% (95% CI: 34.7–44.8%)) had sought medical attention for this reason, with the health-care professional being consulted and the mean number of visits reported in the previous year shown in **Supplementary Table S2**. In 56 cases (39.2% (95% CI: 20.0–34.6%)) some kind of test was performed: 39 blood test, 11 barium enemas, and 24 colonoscopies were reported by these subjects.

When symptoms of CC were analyzed in subjects who had consulted a health-care professional and compared against those in subjects who had made no such consultation, consulters were found to have significantly more instances of harder stools, straining, incomplete evacuation, anal blockage, digitation, and abdominal pain than did nonconsulters (**Figure 3**). In the multivariate model, symptoms independently associated with consultation owing to constipation were abdominal pain (OR = 2.1 (1.2–3.6)) and digitation (OR = 2.1 (1.3–3.3)).

One hundred and seventy subjects from the study population (11.3% (9.7-12.9)) reported using laxatives in the preceding year. As shown in Table 2, patients with painful CC or CC in patients with IBS took more laxatives than did subjects with nonpainful CC (50, 67, and 31%, respectively). Of those using laxatives, 82 (48%) patients were completely satisfied with the results, 52 (30.6%) were somewhat satisfied, whereas 36 (21.2%) were dissatisfied. Abdominal symptoms related to laxative use were frequent: 16.5% reported abdominal pain, 7.1% reported bloating, 10.6% reported diarrhea, and 5.3% reported other symptoms. Patients with non-painful CC were completely satisfied more frequently (44%) than were patients with painful CC (20%) or CC in patients with IBS (31%). However, abdominal pain related to laxative use was significantly more frequent (P < 0.01) in patients with painful CC (53%) and nonpainful CC (23%) than in CC in patients with IBS (6%). No differences in other laxative-related symptoms were found among these subgroups of constipation.

Quality of life. Subjects with CC showed significant impairment in the physical (48.1 ± 10.5 vs. 51.0 ± 8.8 ; P<0.001) and mental components (47.9 ± 10.3 vs. 52.3 ± 9.8 ; P<0.001) of the SF-12 questionnaire compared with subjects without constipation. According to the CVE-20 questionnaire, no statistically significant difference in constipation-related quality of life was found among subgroups (nonpainful CC (49.2 ± 16.1), painful CC (44.4 ± 9.4), and CC in patients with IBS (47.2 ± 13.2)).

DISCUSSION

Our study reports the results of a community survey focused on three aspects: the spectrum of constipation, risk factors for constipation, and burden of constipation.

The spectrum of constipation

The concept of constipation is related to bowel habit, including frequency, consistency, and defecatory symptoms, regardless of the criteria or consensus consulted. However, subjects with CC may report abdominal bloating or discomfort. Thus, CC may overlap with IBS. In fact, in clinical practice, it may be difficult to differentiate between CC and IBS accurately and reliably.

Currently, separation of IBS and CC as two different entities is warranted by an exclusive criterion in Rome III consensus. This separation may be supported by studies using cluster analysis. Talley *et al.* (27) evaluated whether independent, digestive symptom-based subgroups exist in four countries in line with the Rome criteria. All countries reported symptom groupings described with IBS and constipation, and as dyspepsia and/or gastroesophageal reflux, as well as a healthy group. Among IBS subjects, subgrouping into diarrhoea-predominant, constipation-predominant, and

Table 3. Sociodemographic spectrum of constipation

	Nonpainful CC (N=209)	Painful CC (N=30)	CC in patients with IBS (N=49)	Ρ
BMI				
Normal (<25 kgm ⁻²) (<i>n</i> (%))	116 (56)	23 (77)	29 (59)	0.3
Overweight (25–29.9 kg m ⁻²) (<i>n</i> (%))	63 (30)	4 (13)	14 (29)	
Obesity (30 kg m^{-2} or more) (n (%))	29 (14)	3 (10%)	6 (12)	
Marital status				
Married (<i>n</i> (%))	136 (65)	20 (67)	26 (53)	0.4
Single (<i>n</i> (%))	44 (21)	8 (27)	14 (29)	
Others (<i>n</i> (%))	29 (14)	2 (7)	9 (18)	
Educative level				
Primary (<i>n</i> (%))	77 (37)	8 (27)	14 (29)	0.7
Secondary (n (%))	71 (34%)	11 (37)	20 (41)	
University (n (%))	61 (29)	11 (37)	15 (31)	
Geographical area				
Mediterranean (n (%))	130 (62)	17 (57)	28 (57)	0.2
Center (<i>n</i> (%))	56 (27)	12 (40)	12 (24)	
Atlantic (n (%))	23 (11)	1 (3)	9 (18)	
Habitat				
Rural (<i>n</i> (%))	42 (20)	8 (27)	7 (14)	0.4
Urban (<i>n</i> (%))	167 (80)	22 (73)	42 (86)	
Liquid intake (glasses of liquid daily)				
First quintile (7 glasses or less) (n (%))	57 (27)	12 (40%)	10 (20)	0.6
Second quintile (8–9 glasses) (n (%))	45 (21)	8 (27)	10 (20)	
Third quintile (10–11 glasses) (n (%))	44 (21)	4 (13)	10 (20)	
Fourth quintile (12–14 glasses) (n (%))	37 (18)	4 (13)	10 (20)	
Last quintile (15 glasses or more) (n (%))	26 (12)	2 (7)	9 (19)	
Fiber intake (grams daily)				
First quintile (<i>n</i> (%))	52 (25)	5 (17)	11 (22)	0.2
Second quintile (n (%))	39 (19)	7 (23)	13 (26)	
Third quintile (<i>n</i> (%))	34 (16)	3 (10)	9 (18)	
Fourth quintile (n (%))	39 (19)	11 (37)	5 (10)	
Last quintile (n (%))	45 (21)	4 (13)	11 (22)	
Physical exercise (self-reported)				
Do sports regularly (n (%))	42 (20)	2 (7)	9 (18)	0.5
Long walks (n (%))	53 (25)	11 (37)	15 (31)	
Short walks (n (%))	88 (42)	12 (40)	21 (43)	
Not used to walking regularly $(n (\%))$	26 (12)	5 (17)	4 (8)	
BMI, body mass index; CC, chronic constipation.				

alternating bowel habit is supported, not only by Rome criteria but also by a study that used cluster analysis and found marked differences across the three groups, suggesting that each may have a different pathogenesis and respond to different treatment approaches (28). Nevertheless, it is unclear whether IBS patients with CC are closer to CC or to other subgroups of IBS.

Although relatively few studies identified in the literature search collected data on prevalence of CC according to IBS symptom



Figure 3. Symptoms of CC in subjects who consulted a health-care professional compared with subjects who did not. CC, chronic constipation.

status, the five studies that did so reported a marked increase in the prevalence of CC in subjects with IBS as compared with those without IBS (29-33). The issue of overlap between IBS and CC was examined in detail in a recent study that assessed the ability of the Rome III criteria to distinguish between the two disorders (20). The authors suspended the mutual exclusivity of the two sets of diagnostic criteria and reported that this led to a significant overlap between them, and a lack of stability in the respective diagnosis during follow-up, suggesting that IBS and CC are not entirely separated. The authors conclude that IBS-C and CC may be different subgroups within the same disorder. The fact that newer therapies effective for the treatment of CC, such as lubiprostone or linaclotide (14,17,34), appear to be of benefit in IBS-C (18,35,36) also supports that theory. Similarly, our data also showed that community subjects with IBS-C are close to subjects with CC in terms of laxative use, impact on the quality of life, and constipation symptoms. Moreover, it seems that painful CC and IBS-C represent the more severe part of a spectrum, with sufferers being more likely to regard themselves as constipated, consult, use laxatives, and report more symptoms of constipation. Paradoxically, therefore, IBS-C patients tend to be more constipated than patients with constipation.

Factors associated with CC.

Our study observed a remarkable higher prevalence of CC among women (2.7:1 ratio), a finding in line with a previous study in Spain (10) and a recent meta-analysis (7). Prevalence also showed a slight trend to increase with age for the whole population, mainly owing to an increase among men, suggesting different underlying mechanisms for constipation in men and women. Within Spain, geographical differences were in evidence, with the highest prevalence in the Mediterranean area and the lowest in the Atlantic area; although not relevant in the multivariate analysis, one could speculate that differences in climate (warmer areas with higher prevalence) might be responsible for this. However, geographical relevance in CC is beyond the scope of this study. No worldwide geographical differences were found in the recent meta-analysis mentioned above (7).

Our study analyzed some lifestyle factors related to CC. It is interesting to note that prevalence of CC increased with decreasing liquid intake, in men and women alike; despite the usual recommendation to increase liquid intake in the treatment of CC, there is little evidence indicating an association between liquid intake and constipation. Markland et al. (37), on the basis of data on more than 10,000 adults of the National Health and Nutrition Examination Surveys, recently reported that low liquid consumption is a predictor of constipation among women and men. Low fiber intake is a recognized risk factor for constipation, and recent decades have seen increased fiber consumption being promoted in the media as a healthy habit. We found a U-shaped association between constipation and fiber intake (more constipation with smaller and greater amounts). In the study by Markland et al. (37), however, dietary fiber was not a predictor of constipation. Physical activity was inversely associated with CC prevalence, which is in line with previous studies (38). Moreover, this was the only lifestyle habit associated with constipation in the multivariate analysis, underscoring its relevance as a risk factor. Although promoting physical exercise has not been shown to improve constipation (39), our data would nonetheless support this recommendation being added to the usually recommended lifestyles changes.

Burden of constipation

Constipation has been shown to have a remarkable economic (40,41) and personal impact (42). Around 40% of subjects who regarded themselves as constipated had sought health-care advice (mostly from primary care physicians and gastroenterologists) in the preceding year for this reason. This figure is close to that published by Garrigues *et al.* (10) in Spain. The workload entailed for the health system may be estimated as ~243 medical visits (165 to primary care physicians and 78 to gastroenterologists) and 16 colonoscopies per 1,000 inhabitants over 18 years per annum.

Among the characteristics of constipation associated with consultation, two interesting finding emerged. First, infrequent defecation was not clearly associated with consultation, thus emphasizing the perceived importance of the remaining symptoms for subjects who regard themselves as constipated. Second, the symptoms more associated with consultation were digitation, which may reasonably impel a subject to seek medical advice, and pain, which is not conceptually a symptom of constipation, adding support to the theory that there is a real spectrum of CC.

Laxatives were used by more than 10% of our evaluated population, a figure similar to that of other community studies (43), but only about 50% of such subjects were completely satisfied with their use. Similar findings have been reported by another recent European study (44). Moreover, laxatives are associated with a considerable amount of side effects, although there is a lack of data on these side effects in the community. This study indicates that over 10% of subjects taking laxatives report diarrhea and 16% report abdominal pain. Our data thus add more evidence to show that there is a gap in the treatment of CC, particularly among patients with painful CC and IBS-C.

In conclusion, CC appears to be a spectrum: most patients do not have abdominal pain/discomfort but others (with otherwise quite similar characteristics) are patients with IBS or fall outside any established diagnosis. Among the risk factors for CC, physical exercise is a modifiable factor that should be recognized. CC generates a considerable workload for primary care physicians and gastroenterologists, and laxatives only partially meet patients' needs, especially in the case of those with painful CC and associated IBS.

CONFLICT OF INTEREST

Guarantor of the article: Enrique Rey, MD, PhD.

Specific author contributions: Study concept and design, analysis and interpretation of data, and drafting of the manuscript: Enrique Rey, Fermín Mearin; analysis and interpretation of data, and drafting of the manuscript: Agustín Balboa.

Financial support: None.

Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- In chronic constipation (CC), abdominal pain/discomfort are symptoms not included in the definition, but some patients with constipation have abdominal pain/discomfort without fulfilling criteria for irritable bowel syndrome (IBS).
- We compared clinical and epidemiological aspects of nonpainful CC, painful CC, and CC in patients with IBS.

WHAT IS NEW HERE

- Subjects with painful CC and CC with IBS were younger, reported more constipation, and had more symptoms than subjects with nonpainful CC.
- ✓ Following multivariate adjustment, we found that CC can be associated with age and physical activity.
- CC appears to be a spectrum: most patients do not have abdominal pain/discomfort, but others (with otherwise quite similar characteristics) are patients with IBS or fall outside any established diagnosis.

REFERENCES

- Stewart WF, Liberman JN, Sandler RS *et al.* Epidemiology of constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. Am J Gastroenterol 1999;94:3530–40.
- Higgins PD, Johanson JF. Epidemiology of constipation in North America: a systematic review. Am J Gastroenterol 2004;99:750–9.
- Johanson JF, Kralstein J. Chronic constipation: a survey of the patient perspective. Aliment Pharmacol Ther 2007;25:599–608.
- Talley NJ, Fleming KC, Evans JM *et al.* Constipation in an elderly community: a study of prevalence and potential risk factors. Am J Gastroenterol 1996;91:19–25.
- Hungin AP, Whorwell PJ, Tack J *et al.* The prevalence, patterns and impact of irritable bowel síndrome: an international survey on 40000 subjects. Aliment Pharmacol Ther 2003;17:643–50.
- Choung RS, Locke GR III. Epidemiology of IBS. Gastroenterol Clin North Am 2011;40:1–10.
- 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;106:1582–91.
- Mearin F, Badía X, Balboa A *et al.* Irritable bowel syndrome prevalence varies enormously depending on the employed diagnostic criteria: comparison of Rome II versus previous criteria in a general population. Scand J Gastroenterol 2001;36:1155–61.

- 9. Sperber AD, Shvartzman P, Friger M *et al.* A comparative reappraisal of the Rome II and Rome III diagnostic criteria: are we getting closer to the 'true' prevalence of irritable bowel syndrome? Eur J Gastroenterol Hepatol 2007;19:441–7.
- Garrigues V, Gálvez C, Ortiz V *et al.* 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;159:520–6.
- Longstreth GF, Thompson WG, Chey WD et al. Functional bowel disorders. Gastroenterology 2006;130:1480–91.
- Kamm MA, Müller-Lissner S, Talley NJ et al. Tegaserod for the treatment of chronic constipation: a randomized, double-blind, placebo-controlled multinational study. Am J Gastroenterol 2005;100:362–72.
- Novick J, Miner P, Krause R *et al.* A randomized, double-blind, placebocontrolled trial of tegaserod in female patients suffering from irritable bowel syndrome with constipation. Aliment Pharmacol Ther 2002;16:1877–88.
- 14. Johanson JF, Morton D, Geenen J *et al.* Multicenter, 4-week, double-blind, randomized, placebo-controlled trial of lubiprostone, a locally-acting type-2 chloride channel activator, in patients with chronic constipation. Am J Gastroenterol 2008;103:170–7.
- 15. Drossman DA, Chey WD, Johanson JF *et al.* Clinical trial: lubiprostone in patients with constipation-associated irritable bowel syndrome—results of two randomized, placebo-controlled studies. Aliment Pharmacol Ther 2009;29:329–41.
- Ford A, Brandt L, Young C *et al.* Efficacy of 5-HT3 antagonists and 5-HT4 agonists in irritable bowel syndrome: systematic review and meta-analysis. Am J Gastroenterol 2009;104:1831–43.
- Lembo AJ, Schneier HA, Shiff SJ *et al.* Two randomized trials of linaclotide for chronic constipation. N Engl J Med 2011;365:527–36.
- Johnston JM, Kurtz CB, MacDougall JE et al. Linaclotide improves abdominal pain and bowel habits in a phase IIb study of patients with irritable bowel syndrome with constipation. Gastroenterology 2010;139:1877–86.
- Drossman DA, Morris C, Hu Y *et al*. Further characterization of painful constipation (PC): clinical features over one year and comparison with IBS. J Clin Gastroenterol 2008;42:1080–8.
- Wong RK, Palsson OS, Turner MJ *et al.* Inability of the Rome III criteria to distinguish functional constipation from constipation-subtype irritable bowel syndrome. Am J Gastroenterol 2010;105:2228–34.
- Drossman DA, Corazziari E, Delvaux M *et al*. Apéndice B: Criterios diagnósticos de Roma III para los trastornos funcionales gastrointestinales. Rev Gastroenterol Mex 2010;75:511–6.
- 22. Moreno Elola-Olaso C, Rey E, Rodríguez-Artalejo F *et al.* Adaptation and validation of a gastroesophageal reflux questionnaire for use on a Spanish population. Rev Esp Enf Digest 2002;94:745–51.
- Alonso J, Regidor E, Barrio G *et al.* Valores poblacionales de referencia de la versión española del Cuestionario de Salud SF-36. Med Clin Barc 1998;111:410–6.
- Barceló M, Jimenez-Cebrian MJ, Díaz-Rubio M et al. Validation of a questionnaire for assessing fecal impaction in the elderly: impact of cognitive impairment, and using a proxy. BMC Geriatr 2013;13:24.
- Badia X, Mearin F, Balboa A *et al.* Burden of illness in irritable bowel syndrome comparing Rome I and Rome II criteria. Pharmacoeconomics 2002;20:749–58.
- Perona M, Mearin F, Guilera M *et al.* Quality of life specific questionnaire for constipated patients: development and validation of CVE-20. Med Clin (Barc) 2008;131:371–7.
- 27. Talley NJ, Holtmann G, Agréus L *et al.* Gastrointestinal symptoms and subjects cluster into distinct upper and lower groupings in the community: a four nations study. Am J Gastroenterol 2000;95:1439–47.
- 28. Guthrie E, Creed F, Fernandes L *et al.* Cluster analysis of symptoms and health seeking behaviour differentiates subgroups of patients with severe irritable bowel syndrome. Gut 2003;52:1616–22.
- Talley NJ, Zinsmeister AR, Van Dyke C *et al.* Epidemiology of colonic symptoms and the irritable bowel syndrome. Gastroenterology 1991;101:927–34.
- 30. Jones R, Lydeard S. Irritable bowel syndrome in the general population. Br Med J 1992;304:87–90.
- Locke GR III, Zinsmeister AR, Fett SL *et al.* Overlap of gastrointestinal symptom complexes in a US community. Neurogastroenterol Motil 2005;17:29–44.
- Sorouri M, Pourhoseingholi MA, Vahedi M *et al.* Functional bowel disorders in an Iranian population using Rome III criteria. Saudi J Gastroenterol 2010;16:154–60.

- Koloski NA, Talley NJ, Boyce PM. Epidemiology and health care seeking in the functional GI disorders: a population-based study. Am J Gastroenterol 2002;97:2290–9.
- Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in chronic idiopathic constipation: systematic review and meta-analysis. Gut 2011;60:209–18.
- Johanson JF, Drossman DA, Panas R *et al.* Clinical trial: phase 2 study of lubiprostone for irritable bowel syndrome with constipation. Aliment Pharmacol Ther 2008;27:685–96.
- Manabe N, Rao AS, Wong BS *et al.* Emerging pharmacologic therapies for irritable bowel syndrome. Curr Gastroenterol Rep 2010;12:408–16.
- 37. Markland AD, Palsson O, Goode PS *et al*. Association of low dietary intake of fiber and liquids with constipation: evidence from the National Health and Nutrition Examination Survey. Am J Gastroenterol 2013;108:796–803.
- Dukas L, Willett WC, Giovannucci EL. Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. Am J Gastroenterol 2003;98:1790–6.

- Locke GR III, Pemberton JH, Phillips SF. AGA technical review on constipation. American Gastroenterological Association. Gastroenterology 2000;119:1766–78.
- Singh G, Lingala V, Wang H et al. Use of health care resources and cost of care for adults with constipation. Clin Gastroenterol Hepatol 2007;5:1053–8.
- Choung RS, Branda ME, Chitkara D *et al.* Longitudinal direct medical costs associated with constipation in women. Aliment Pharmacol Ther 2011;33:251–60.
- Belsey J, Greenfield S, Candy D *et al.* Systematic review: impact of constipation on quality of life in adults and children. Aliment Pharmacol Ther 2010;31:938–49.
- 43. Gálvez C, Garrigues V, Ortiz V *et al.* Healthcare seeking for constipation: a population-based survey in the Mediterranean area of Spain. Aliment Pharmacol Ther 2006;24:421–8.
- Müller-Lissner S, Tack J, Feng Y *et al.* Levels of satisfaction with current chronic constipation treatment options in Europe - an internet survey. Aliment Pharmacol Ther 2013;37:137–45.