RUNNING TITLE: DETAIL questionnaire multicentric validation

Full-length article

Title: Multicenter validation of the DETAIL questionnaire for the screening of spondyloarthritis in patients with inflammatory bowel diseases

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Abstract

Background: Spondyloarthritis (SpA) is among the most frequent extra-intestinal manifestations in inflammatory bowel diseases (IBD). In this study, we aimed to validate the DETection of Arthritis in Inflammatory bowel diseases (DETAIL) questionnaire in a multicenter cohort of IBD patients enrolled at eleven Gastroenterology Units.

Methods: From October 2018 to March 2019, consecutive adult patients with IBD, either Crohn's disease or ulcerative colitis, filled out independently the DETAIL in the outpatient waiting room. Within two weeks a blinded rheumatologist assessed all the patients, irrespectively of the DETAIL results, and classified them to be affected or not by SpA. The performance of the items was evaluated trough Bayesian analysis.

Results: Overall, 418 IBD patients filled out the DETAIL questionnaire. Upon rheumatological evaluation, 102 (24.4%) patients received a diagnosis of SpA. Of the six questions, the best performances were found in item 6 (LR+ 3.77), reporting inflammatory back pain at night, and in item 3 (LR+ 3.31), exploring Achilles enthesitis. The presence of back pain lasting more than three months (LR+ 2.91), of back pain with inflammatory features (LR+ 2.55) and a history of dactylitis (LR+ 2.55), showed also a fairly good performance, whereas a history of peripheral synovitis was slightly worse (LR+ 2.16). The combination of at least three items answered affirmatively yields a post-test probability of SpA of 80% or more. The presence of alternative diagnoses, such as osteoarthritis or fibromyalgia, represented a minor confounder.

Conclusions: The DETAIL questionnaire is a useful tool for the early detection of SpA in IBD.

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Introduction

Inflammatory bowel disease-associated spondyloarthritis (SpA/IBD) is a systemic disease characterized by the chronic inflammation of both the gastrointestinal tract and the musculoskeletal system [1]. Inflammatory bowel diseases (IBD), namely Crohn's disease (CD) and ulcerative colitis (UC), are among the most frequent extra-articular complications that may occur in patients with spondyloarthirits (SpA), and, similarly, arthritis is the most frequent extraintestinal manifestation in IBD and may develop before, simultaneously with, or after the diagnosis of overt intestinal disease [2].

The spectrum of the clinical features of the inflammatory articular involvement in IBD is broad, showing patterns of pure spinal involvement (axial SpA [axSpA], including both ankylosing spondylitis [AS], and non-radiographic axial SpA [nr-axSpA]), and patterns of exclusive peripheral arthritis and/or enthesitis [3].

The prevalence of SpA in IBD patients ranges from 4% to 23%, based on different studies [1]. A recent systematic review estimated that axSpA affects 13% of IBD patients, in 10% as isolated sacroiliitis or nr-axSpA and in 3% as overt AS, whereas peripheral arthritis involves about 13% of IBD patients [4]. Additionally, a recent study with a long follow-up reported that, 20 years after IBD diagnosis, the prevalence of AS was 4.5% and of axSpA 7.7%, while one out of four patients developed peripheral SpA [5][6]. Importantly, the prevalence of axial involvement may be underestimated in patients with IBD, since a subclinical sacroiliitis has been observed in around 16% of the IBD patients [7][8].

Despite the well-known relationship between gut and joint inflammation, the availability of the Assessment of SpondyloArthritis international Society (ASAS) classification criteria [9] and the more common use of accurate diagnostic techniques, such as magnetic resonance imaging (MRI) and ultrasonography (US), the diagnostic delay of SpA/IBD is still important, especially for patients with axial involvement, in which it ranges from 5 to 10 years [10][11][12]. The reasons of such a delay are various, from clinicians not always querying

the patients about joint complaints, to patients themselves, underreporting symptoms often misinterpreted as non-specific mechanical joint or back pain [13].

The presence of such an unfavourable diagnostic delay, which often translates into a serious impact on work ability and social participation and several other domains of the quality of life [14][15], drives the need for a proper screening strategy. For example, the availability of accurate biomarkers could be useful to intercept earlier the onset of disease. However, to date, the quest for biomarkers in SpA/IBD has been largely unsatisfactory [16]. A dedicated referral strategy is another tool that could be implemented for such a task. Although during the last decade several referral models for axSpA have been proposed [17][18][19], only a few have been specifically dedicated to SpA/IBD [20][21]. Additionally, most of these strategies focus on axial disease and do not adequately consider peripheral manifestations.

Keeping in mind these issues, we recently developed and preliminarly validated a new self-administered screening tool, called DETection of Arthritis in Inflammatory boweL diseases (DETAIL) questionnaire, to recognize signs and/or symptoms of peripheral and/or axial inflammatory involvement in patients suffering from IBD not previously diagnosed as having a SpA [22].

In this multicenter study, conducted at eleven tertiary referral hospitals located in Italy, we aimed to further validate the DETAIL questionnaire in an independent cohort of IBD patients.

Materials and Methods

DETAIL questionnaire development and preliminary validation

Briefly, the DETAIL instrument has been developed as follows. In May 2016, the Authors (DB, MML, MDC and FS) identified a list of items from the already existing referral models for axSpA, with the goal to develop a 5-8 items questionnaire, with dichotomous answer,

to be filled in quickly in the waiting room of the Gastroenterology Units, easy to understand, and without the need of laboratory or imaging tests. After the elimination of duplicates, of composite questions, of the items requiring figures or special equipments, a list of 30 item was drawn up and then, from June 2016 to October 2016, 95 experts in the field of SpA or IBD rated the importance of each of the 30 items/questions for the detection of signs or symptoms articular or spinal inflammation. Items were retained in the DETAIL questionnaire if they satisfied at least a mean score of 2 on a 0 to 3 Likert scale, and if were rated as quite relevant or very relevant at least by the 70% of the experts. The questions that satisfied the criteria for the inclusion in the final questionnaire (frequency >70% and mean relevance score >2.0) were six.

In October 2016 the final version of the DETAIL questionnaire, made by the six top rated items, was available (Table 1). The English version was translated in Italian, then translated back in English by a mother tongue English speaker.

Thereafter, from October 2016 to April 2017 a pilot testing was conducted at three gastroenterology units. In the preliminary validation, the DETAIL questionnaire showed a good overall accuracy for the referral of IBD patients. In particular, among the six items the best positive likelihood ratio (LR+) was found in item 2 (LR+ 3.82), exploring dactylitis, and in item 6 (LR+ 3.82) and item 5 (LR+ 3.40), two questions exploring inflammatory low back pain. Enthesitis (item 3 - LR+ 2.87) and peripheral synovitis (item 1 - LR+ 2.81) gave similar results, while item 4, exploring the duration of low back pain, resulted in the worst performance (LR+ 1.99) [22].

Multicenter validation

The present study was conducted at eleven tertiary referral centers for IBD, all in Italy. The inclusion criteria were as follows: patients with a diagnosis of IBD (according to the validated criteria [23][24]), aged >18 years, without a previous diagnosis of SpA, able to read and

understand Italian language. Subjects suffering from active cancer or lymphoproliferative disease, uncontrolled diabetes, unstable ischemic heart disease or congestive heart failure, acute renal failure, and those already diagnosed with inflammatory or crystal-induced arthropathies (including gout and calcium pyrophosphate dehydrate deposition disease) were excluded.

Patients were enrolled consecutively and asked to fill in the questionnaire in paper format before the gastroenterological visit. The study was explained by a specifically trained nurse, that also collected informed consent and answered the possible questions of the patient.

Thereafter, within two weeks from the completion of the questionnaire, a trained rheumatologist assessed all the patients, irrespectively of and blinded to all the answers given to the DETAIL questions. The rheumatologic assessment was conducted according to a standard protocol, comprehensive of a complete history and physical examination (tender and swollen joint counts on the 68 and 66 joints, cervical rotation, tragus-to-wall distance, lumbar lateral flexion, modified Schober's test, intermalleolar distance), and laboratory assessment (acute phase reactants, RF, ANA, anti-CCP and HLA B-27, if needed). X-rays, MRI, and US were performed if needed. The rheumatologists were required to confirm that patients with a clinical diagnosis of SpA also fulfilled the ASAS criteria [9], and, if appropriate, to diagnose the presence of other muskuloskeletal disorders.

The study has been approved by the Institutional Review Board of the coordinating centre (Comitato Etico Regionale delle Marche, n°20170206/5362) and by all the local ethics committes. The study was conducted in compliance with the principles of the Declaration of Helsinki. All patients were requested to sign a written informed consent.

Statistical analysis

Baseline demographic and clinical characteristics were recorded for all patients and transferred to an anonymous database. Mode imputation was used to handle missing data.

The performance of the DETAIL questionnaire was evaluated through the calculation of the post-test probability of disease. The post-test probability evaluation of a screening questionnaire is allowed by the knowledge of sensitivity, specificity, and the pre-test probability (the prevalence of the disorder). In this study, the post-test probability was calculated using the Bayesian Analysis Model method, defining for each item of the questionnaire the positive likelihood ratio (LR+), and with the graphics representation on the Fagan's nomogram. In this nomogram, a straight line drawn from a patient's pre-test probability of disease through the total LR+ of the test (given by the LR+ product of the items answered as "yes" in the questionnaire) will intersect with the post-test probability of disease on the right axis.

Results

Patients

From October 2018 to March 2019, 418 consecutive adult patients with IBD (211 F; 203 CD, 209 UC, 6 indeterminate colitis; mean age 49.7±14.4 y, median duration of IBD 10 y) filled out independently the DETAIL questionnaire in the waiting room of the Gastroenterology Unit outpatient clinics.

Upon rheumatologic assessment, 102 (24.4%) patients fulfilling the ASAS criteria were classified as SpA/IBD (Figure 1). This percentage represents the prevalence of SpA in our IBD cohort and therefore our pre-test probability.

Patients' demographic and clinical characteristics are summarized in Table 2. There were no differences in the two groups, except for a higher proportion of women in the SpA/IBD cohort (60.7% vs 47.1%) and a slightly higher number of SpA/IBD patients taking corticosteroids.

Among patients with SpA/IBD, the median duration of joint complaints was 5 years (min 0, max 30). Fifty-eight patients (56.9%) were classified as axSpA, with or without concomitant peripheral involvement (18 patients), while 44 (43.1%) subjects with arthritis and/or enthesitis and/or dactylitis were classified as peripheral SpA. Among these patients, enthesitis was present in 26 subjects (25.5%), whereas dactylitis only in 3 patients (3%). A concomitant fibromyalgia (FM) was present in 4 (4%) patients with SpA/IBD.

With regard to SpA disease activity, the mean ASDAS score was 3.0 ± 1.2 and the mean BASDAI score was 4.3 ± 2.0; mean CRP levels were 1.0 ± 1.5 mg/dl.

Alternative diagnoses

Among IBD patients without SpA, 184 patients (58.2%) reported musculoskeletal complaints. The median number of affirmative responses to the DETAIL question in this group was 1 (min 0, max 6). The most frequent alternative diagnosis was represented by osteoarthritis (OA) (142 subjects, 33.9% of the whole cohort), in particular lumbar spine OA in 65 patients and peripheral OA in 77 subjects. In 22 patients (5.2% of the whole cohort), a diagnosis of FM was made. Ten participants had an isolated tendinitis, 8 received a diagnosis of aspecific muscle and joint pain, one had gout, and one a primary Raynaud's phenomenon.

DETAIL replies, feasibility and acceptability

The total number of replies to the DETAIL questions were as follows: a) Question 1: 173 yes, 245 no; b) Question 2: 63 yes, 355 no; c) Question 3: 89 yes, 329 no; d) Question 4: 163 yes, 255 no; e) Question 5: 186 yes, 232 no; f) Question 6: 102 yes, 316 no.

The mean time to fulfill the DETAIL was 46 ± 28 seconds, and it was fully completed by the vast majority of the subjects (less than 2% of questionnaires had missing values).

The majority of the subjects (85.2%) rated the questionnaire easy to understandand and to be filled in.

The percentage of patients with or without SpA replying affirmatively to the single questions is shown in Figure 2A. Figure 2B shows the distribution of the total number of questions answered affirmatively in each group. In detail, among 102 patients with SpA/IBD, 9 answered 6/6 yes, 18 filled in 5/6 yes, 30 put 4/6 yes, 19 answered 3/6 yes, 19 filled in 2/6 yes, and 5 replied 1/6 yes and 2 answered 0/6 yes.

Patients with IBD without a concomitant SpA represented the majority of the cohort (316, 75.6%). Of them, 132 replied 0/6 yes, 72 answered 1/6 yes, 44 put 2/6 yes, 33 filled in 3/6 yes, 24 replied 4/6 yes, 10 answered 5/6 yes, and 1 put 6/6 yes on the DETAIL questionnaire.

Analysis of the DETAIL performance

Applying the Bayesian analysis on the six items of the DETAIL, the best performances in discriminating patients affected or not by SpA were found in question number 6 (LR+ 3.77, 95%CI), reporting inflammatory low back pain at night, and in question number 3 (LR+ 3.31, 95%CI), exploring Achilles enthesitis.

The other two questions exploring the duration of low back pain (LR+ 2.91, 95%CI) and its inflammatory features (LR+ 2.55, 95%CI) had also a fairly good performance for the detection of patients with AxSpA.

A history of dactylitis and the presence of signs and symptoms of peripheral synovitis had an overall slightly worse performance (LR+ 2.55, 95%CI and 2.16, 95%CI, respectively) (Table 3).

Application of the DETAIL questionnaire

The DETAIL instrument is easily applied using the Fagan's nomogram representation. The

product of LR+ of each affirmative answer should be used in order to obtain the probability of SpA in each individual patient, starting from his pre-test probability (the prevalence of the disease). A test is usually considered very useful, i.e. having a large effect on the pre-test probability, if LR+ is equal to 10 or more. For the DETAIL questionnaire, the combination of three or more different items answered affirmatively yields a LR+ of 14 at the least (items 1, 2 and 5). Applying this LR+ to our prevalence of disease, we obtain a post-test probability of 81.9%, which is high enough to warrant referral (Figure 3).

The development of a “DETAIL” application for smartphones, which is ongoing, will allow the automatic and immediate calculation of the post-test probability of disease as soon as the patient answers the questions. Thus, the post-test probability will be readily available on screen to the clinician that, if at least three affirmative answers have been given, will see an highlighted value to mean that referral is strongly indicated.

Discussion

The aim of this study was to validate a recently developed questionnaire for the early detection of signs and symptoms of SpA in patients with IBD, that showed good screening properties in a preliminary study [22].

In this multicenter work, the DETAIL instrument confirmed to be an easy and powerful tool for rheumatologic referral of IBD patients with joint complaints. Briefly, among the 418 IBD patients that underwent screening with the DETAIL instrument, 102 have been diagnosed with SpA/IBD (58 with axSpA and 44 with isolated peripheral SpA), for a pooled prevalence of SpA of 24%, further confirming that articular involvement is among the most frequently reported extra-intestinal manifestations in IBD [1][12]. In our cohort, SpA/IBD patients had a median diagnostic delay of 5 years, and a mean high disease activity according to ASDAS

score. Among SpA/IBD patients who have been diagnosed with axSpA, one out of three also had a concomitant peripheral involvement.

The DETAIL questionnaire is composed of six questions querying both axial and peripheral joint symptoms. Overall, the questions exploring axial disease (items 4 to 6) have a better accuracy compared to those that enquire peripheral involvement. The items exploring enthesitis (item 3) and dactylitis (item 2) are highly specific, though not sensitive, reflecting their lower prevalence in our cohort (6% and less than 1% of the whole cohort, respectively). Compared to a disease in the same spectrum, such as psoriatic arthritis (PsA), the referral of IBD patients with muskoloskeletal involvement is still suboptimal, but the best strategy to achieve an earlier diagnosis of SpA/IBD has not been determined. For example, establishing a multidisciplinary team that provides a simultaneous evaluation improves the global management of both PsA and SpA/IBD patients [12][25][26][27], but it is also true that such a strategy may not be feasible in all the settings, considering the limitations in terms of time and resources. An appropriate strategy should thus optimize the cooperation between gastroenterologists and rheumatologists, referring to each other only the patients with a high probability of disease. Whereas several questionnaires have been proposed and validated as screening tools for PsA [28][29], for SpA/IBD there is a lack of effective instruments. The Toronto Axial Spondyloarthritis Questionnaire in Inflammatory Bowel Disease was developed in 2013 [20], but it was thought to be administered only to patients who have ever had chronic back pain or stiffness persisting for ≥ 3 months and, to our knowledge, a formal validation study has not been conducted yet. Queiro et al proposed two different 3-question surveys, one exploring axial involvement and one peripheral arthritis, a strategy showing promising properties, though in a preliminary study [21].

The DETAIL questionnaire has several important advantages. The strengths of this tool are its easiness, feasibility and accuracy. In fact, the questionnaire can be easily filled in by the patient while waiting for the gastroenterological visit, since it is composed by six simple

questions and does not require any laboratory or imaging tests. Indeed, the use of the Bayesian method allows the clinician to obtain an estimate of the post-test probability of the patient having a SpA in a few seconds. The proposed cut-off of three affirmative answers out of six is not intented to be used categorically, as the results of this screening questionnaire are the first step within a referall strategy that aims to increase the chances that IBD patients seen by the rheumatologist are affected by SpA and, thus, even referral of patients with less than three questions answered positively may be acceptable in some cases. Finally, since the use of Fagan's nomogram in clinical practice is impractical, the availability of an application for smartphones will make such a tool ever easier to use for both patients and physicians.

The ability of the DETAIL to intercept patients at high risk of inflammatory axial involvement is important, as almost half of IBD patients may report back pain, most of the times non-specific or mechanical in nature, during the course of the disease [5]. In fact, the early identification of patients affected by axSpA allows an earlier treatment with effective therapies such as biologic drugs [30]. Compared to the other available questionnaires, the added value of the DETAIL questionnaire is the presence of three items exploring peripheral joint disease, including enthesitis and dactylitis, which are often easily overlooked by the clinicians but constitute a significant cause of morbidity in these patients.

The DETAIL instrument has some potential limitations. First, it may not be able to discriminate between inflammatory, mechanic or neuropathic sources of pain. As such, symptoms from non-inflammatory musculoskeletal diseases may represent minor confounders. Of note, patients with OA usually answered affirmatively only to few questions (less than 3), thereby restricting their immediate referral to the rheumatologist. Conversely, FM should be a concern in every patient that reports widespread pain, since this comorbidity may affect up to 30% of IBD patients [31]. In this subgroup, the DETAIL questionnaire is likely less useful. However, even if they are referred, the rheumatologist should be able to

discriminate between inflammatory pain and central sensitization and make a proper diagnosis [32]. Concomitant psoriasis is another potential confounder, since joint symptoms in this population of IBD patients may represent the expression of a PsA, whether if known or not. Albeit it may reduce the specificity of the questionnaire, the referral of some PsA patients could be expected and thus they should be managed accordingly.

The study has some limitations as well. First, the clinical assessment of SpA may reflect the local clinical practice, as it was made by different rheumatologists in various tertiary referral centers. These issues were addressed by using i) blinding, ii) a standardized procedure for the rheumatological assessment and iii) the use of ASAS classification criteria for the diagnosis of SpA. Second, it is possible that patients with subclinical sacroiliitis have been misclassified, since our screening strategy is based on symptoms and MRI was not systematically performed in all subjects. In this regard, we cannot exclude the risk of overdiagnosis, given the known limitations of bone marrow edema in the definition of active sacroiliitis.

In conclusion, we developed and validated the DETAIL instrument, a new screening tool for the detection of SpA, in a large multicenter IBD cohort. The DETAIL is a 6-item questionnaire that allows the immediate calculation of the probability of having a SpA/IBD and thus it will surely represent an important instrument for the screening and the rheumatologic referral of IBD patients.

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Figure legends

Figure 1. Flow-chart showing the characteristics of the inflammatory bowel disease patients diagnosed with spondyloarthritis.

Figure 2. Distribution of the replies to the DETAIL questionnaire. Panel A shows the percentage of patients with or without SpA answering affirmatively to each question (from question 1 (Q1) to question 6 (Q6). Panel B show the distribution of the total number of questions anwered affirmatively in each group, from six to zero.

Figure 3. Application of the DETection of Arthritis in Inflammatory boweL diseases (DETAIL) questionnaire. Example of application of the nomogram in the calculation of the post-test probability. The likelihood ratio product of the three questions about peripheral arthritis (item 1), dactylitis (item 2) and back pain with inflammatory features (item 5) is 14, with resultant post-test disease probability of 81.9%.

RUNNING TITLE: DETAIL questionnaire multicentric validation

APPENDIX

List of collaborators

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Table 1. The DETection of Arthritis in Inflammatory bowel diseases (DETAIL) questionnaire for the screening of spondyloarthritis in patients with inflammatory bowel diseases

Questions	Yes	No
1. Have you ever had a finger or a toe and/or another joint swollen and painful for no apparent reason?		
2. Occasionally, has an entire finger or toe becomes swollen, making it look like a 'sausage'?		
3. Have you had pain in your heels?		
4. Have you ever had back pain lasting at least 3 months that was not injury related?		
5. Do you have low back pain in the morning and/or after resting that improves with exercise?		
6. Do you wake up at night because of low back pain?		

Table 2. Clinical and demographic characteristics of the IBD patients according to the diagnosis of SpA

	SpA/IBD (n=102)	IBD without SpA (n=316)
Type of IBD, n (%)		
CD	54 (52.9)	149 (47.2)
UC	45 (44.1)	164 (51.8)
IC	3 (3.0)	3 (1.0)
Female, n (%)	62 (60.7)	149 (47.1)
Age at inclusion (years), mean ± SD	50 ± 12.5	49.5 ± 14.9
IBD duration (years), median (min÷max)	10 (0÷40)	10 (0÷52)
Duration of joint symptoms (years), median (min÷max)	5 (0÷30)	2 (0÷35)
Concomitant psoriasis	5 (4.9)	9 (2.8)
IBD classification*		
Localization CD, n (%)		
L1 (ileal)	23 (42.5)	52 (34.9)
L2 (colonic)	6 (11.1)	21 (14.2)
L3 (ileocolonic)	20 (37.1)	67 (45.1)
L4 (isolated upper disease)	3 (5.6)	4 (2.7)
L1-3+L4	2 (3.7)	5 (1.2)
Behaviour CD, n (%)		
B1 (non-stricturing, non-penetrating)	28 (51.8)	74 (49.7)
B2 (stricturing)	17 (31.5)	50 (33.5)
B3 (penetrating)	3 (5.6)	14 (9.4)
B2+B3	6 (11.1)	11 (7.4)
P (perianal disease)	3 (5.6)	12 (8.0)
Extension UC, n (%)		
E1 (ulcerative proctitis)	5 (11.1)	14 (8.5)
E2 (left-sided UC)	13 (28.9)	73 (44.5)
E3 (extensive UC)	27 (60.0)	77 (47.0)
Current medication use, n (%)		
5-ASA (mesalazine, sulfasalazine, balsalazide)	45 (44.1)	141 (44.6)
Steroids (topical and oral)	12 (11.7)	18 (5.7)
Immunosuppressants (AZA, 6MP, MTX)	8 (7.8)	24 (7.6)
Infliximab	14 (13.7)	67 (21.2)
Adalimumab	19 (18.6)	40 (12.6)
Golimumab	3 (2.9)	6 (1.9)
Ustekinumab	3 (2.9)	6 (1.9)

Vedolizumab	8 (7.8)	28 (8.9)
No therapy	11 (10.8)	30 (9.5)
SpA characteristics		N/A
Axial-SpA, with or without peripheral involvement n(%)	58 (56.9)	
Isolated peripheral-SpA, n(%)	44 (43.1)	
BASDAI, mean ± SD	4.3 ± 2.0	
ASDAS-CRP, mean ± SD	3.0 ± 1.2	
CRP (mg/dl), mean ± SD	1.0 ± 1.5	

*according to the Montreal classification. Abbreviations: IBD: inflammatory bowel disease; SpA: spondyloarthritis; CD: Crohn's disease; UC: ulcerative colitis; IC: indeterminate colitis; ASA: 5-aminosalicylic acid; AZA: azathioprine; 6MP: 6-mercaptopurine; MTX: methotrexate; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score with CRP; CRP: C-reactive protein.

Table 3. Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and post-test probabilities of the six items of the DETAIL questionnaire

Questions	Sensivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
1. Have you ever had a finger or a toe and/or another joint swollen and painful for no apparent reason?	69.6% (59.7%-78.3%)	67.7% (62.2%-72.8%)	41.0% (36.1%-46.0%)	87.3% (83.6-90.3%)	2.16 (1.78-2.65)	0.45 (0.33-0.61)
2. Occasionally, has an entire finger or toe becomes swollen, making it look like a 'sausage'?	27.4% (19.0%-37.1%)	89.2% (85.2%-92.4%)	45.1% (34.4%-56.3%)	79.2% (77.0%-81.2%)	2.55 (1.63-3.99)	0.81 (0.72-0.92)
3. Have you had pain in your heels?	45.1% (35.2%-55.2%)	86.3% (82.1%-89.9%)	51.6% (42.9%-60.3%)	82.9% (80.2%-85.3%)	3.31 (2.33-4.71)	0.64 (0.53-0.76)
4. Have you ever had back pain lasting at least 3 months that was not injury related?	77.4% (68.1%-85.1%)	73.4% (68.1%-78.2%)	48.4% (43.2%-53.7%)	90.9% (87.5%-93.5%)	2.91 (2.36-3.60)	0.31 (0.21-0.44)
5. Do you have low back pain in the morning and/or after resting that	82.3% (73.5%-89.1%)	67.7% (62.2%-72.8%)	45.1% (40.6%-49.7%)	92.2% (88.5%-94.7%)	2.55 (2.12-3.06)	0.26 (0.17-0.40)

improves with exercise?						
6. Do you wake up at night because of low back pain?	54.9% (44.7%-64.7%)	85.4% (81.6%-89.1%)	54.9% (46.9%-62.6%)	85.4% (82.5%-87.9%)	3.77 (2.74-5.19)	0.53 (0.42-0.66)

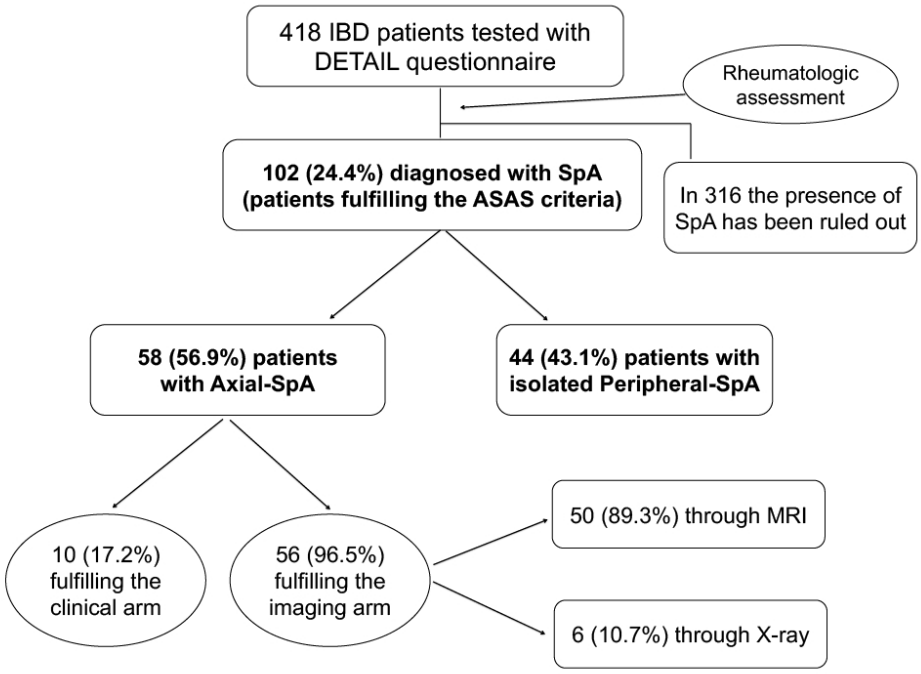

Figure 1. Flow-chart showing the characteristics of the inflammatory bowel disease patients diagnosed with spondyloarthritis.

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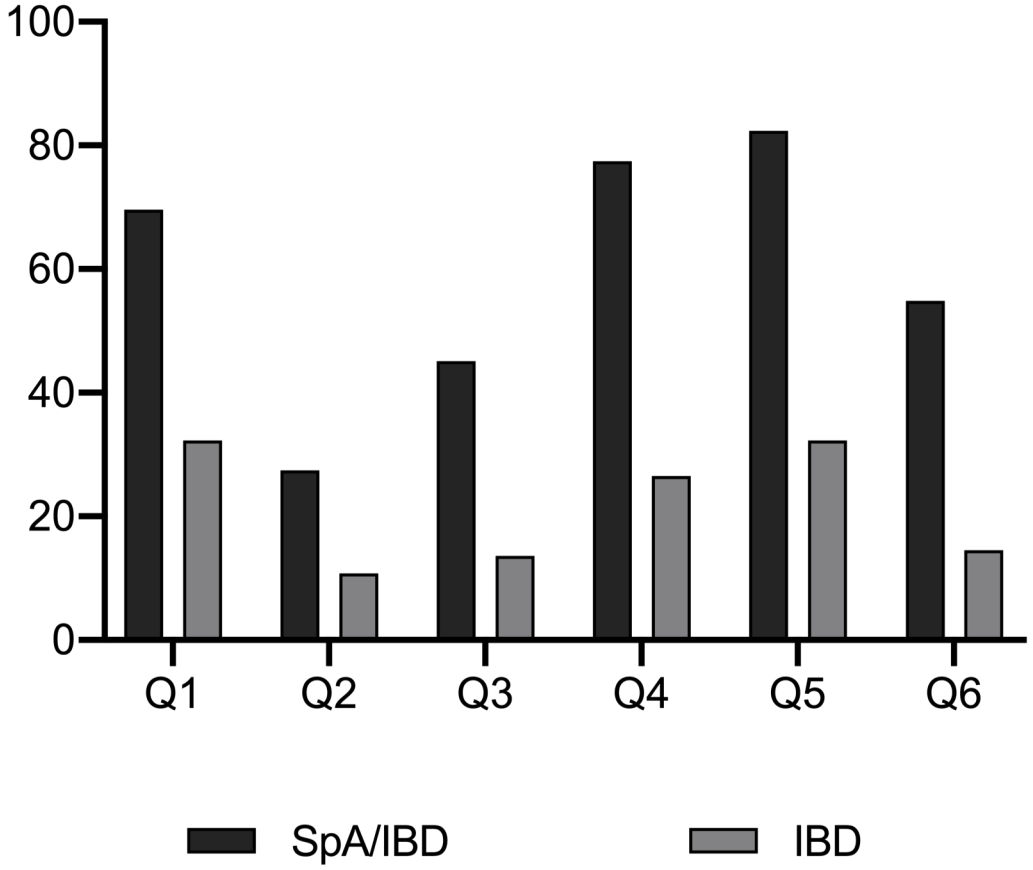

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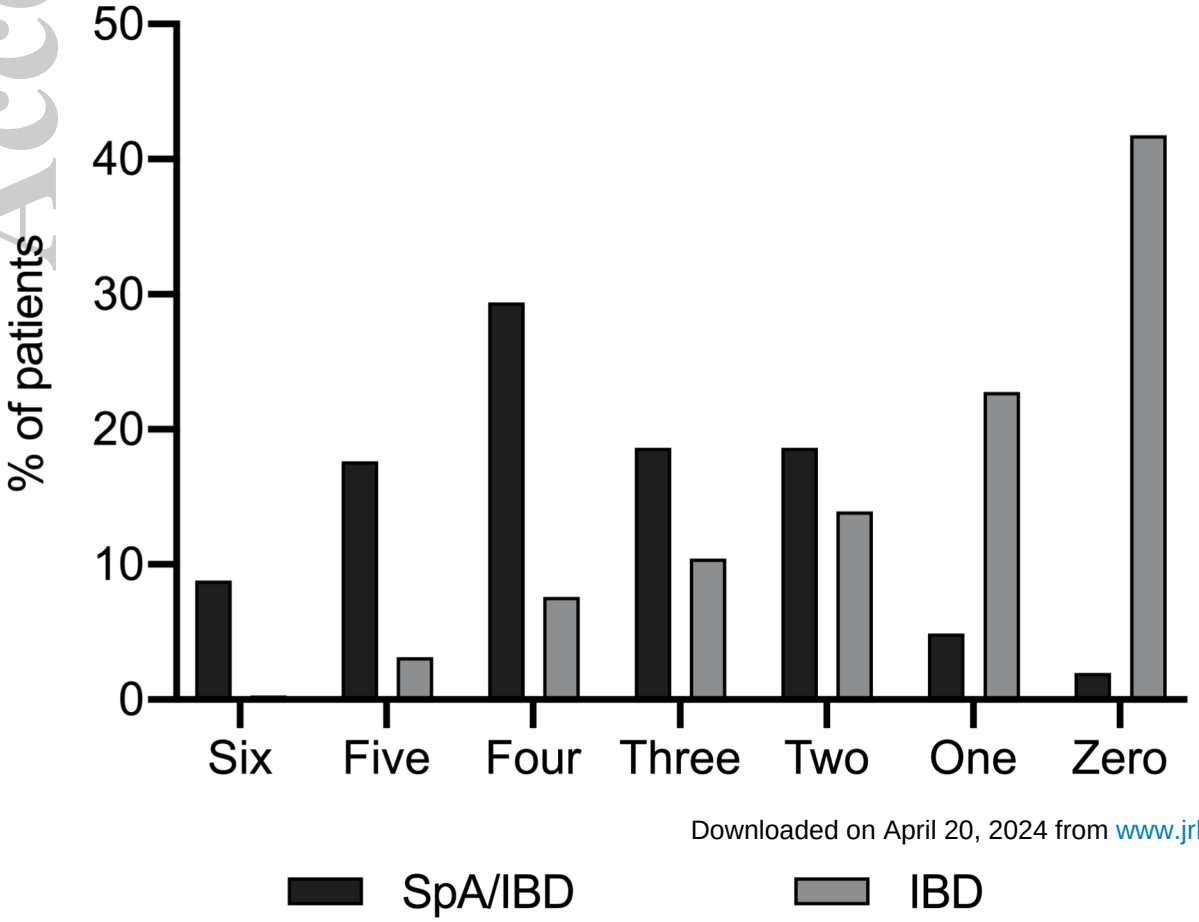

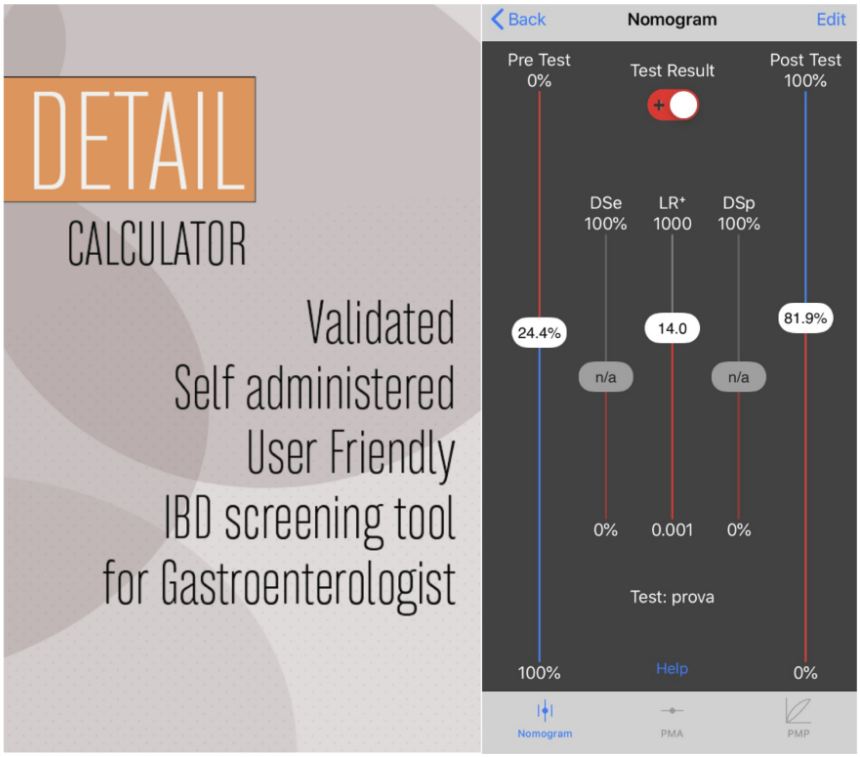

Figure 3. Application of the DETection of Arthritis in Inflammatory boweL diseases (DETAIL) questionnaire. Example of application of the nomogram in the calculation of the post-test probability. The likelihood ratio product of the three questions about peripheral arthritis (item 1), dactylitis (item 2) and back pain with inflammatory features (item 5) is 14, with resultant post-test disease probability of 81.9%.

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