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TITLE: Diagnosis and Management of Inflammatory Bowel Disease Associated Spondyloarthritis

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ABSTRACT

Inflammatory bowel disease (IBD)-associated spondyloarthritis (SpA) is common but remains poorly understood. In this review article, we aim to provide guidance regarding the diagnosis and management of this condition. For diagnosis of IBD-associated peripheral SpA (IBD-pSpA), we recommend collaboration with rheumatology for incorporation of clinical symptoms, physical exam findings, joint imaging if applicable, and available diagnostic criteria. For the management of IBD-pSpA, we first recommend assessment and treatment of underlying luminal IBD disease activity. We provide guidance regarding positioning of advanced therapies for IBD in patients with IBD-pSpA based on the limited available literature. For diagnosis of IBD-associated axial SpA (IBD-axSpA), we recommend rheumatology referral to make the diagnosis based on incorporation of symptoms, laboratory data, imaging findings (sacroiilitis) and available diagnostic criteria. For the management of axial SpA, we recommend co-management with rheumatology and use of either anti-tumor necrosis factor agents or janus kinase inhibitors, when applicable.

Key words: ulcerative colitis, Crohn's disease, joints, spondyloarthritis

INTRODUCTION

Of the extra-intestinal manifestations (EIMs) of inflammatory bowel diseases (IBD), IBD-associated spondyloarthritis (SpA) is among the most common and least well characterized.

The term SpA encompasses inflammatory joint disorders including IBD-associated axial SpA (IBD-axSpA) and peripheral SpA (IBD-pSpA). Prevalence estimates vary but ~30% of patients with IBD have IBD-pSpA and 5% IBD-axSpA.[1] Both can necessitate changes in medical management and negatively impact quality of life in patients with IBD.[2]

Despite high prevalence, literature surrounding diagnosis and management of SpA within the field of IBD remains strikingly limited.[3] Precise, consistent and evidence-based guidance regarding screening and diagnostic strategies and treatment approach is not available due to a lack of high-quality research.[3]

In this review article, our objective is to provide practical guidance to healthcare providers on diagnosis and management of IBD-SpA based on comprehensive analysis of existing literature, albeit limited, supplemented by clinical expertise. Additionally, we outline future directions to improve outcomes and enhance quality of care for patients with IBD-SpA.

DIAGNOSIS

Peripheral SpA

Classification and consensus criteria: There are several classification and consensus criteria available to inform diagnostic approach (Table 1).[3] In the Orchard classification schema, IBD-pSpA is divided into two types.[4] Type I is associated with IBD disease activity, self-limiting (<10 weeks), pauci-articular (<5 joints), asymmetrical and involves large joints.[4] Type II is independent of IBD disease activity, persistent (lasting months/years), polyarticular (≥=5 joints), symmetrical and involves small joints.[4] This schema was developed via a single-center retrospective study, was not prospectively validated, and is not well accepted within rheumatology literature.[3,4] While originally endorsed by gastroenterology literature, guidelines have moved away from these criteria.[5,6] Furthermore, early findings from the Cohort for Healing Arthritis, Skin, and Eye Extra-Intestinal Manifestations (CHASE-EIM), the first multi-center prospective registry of patients with IBD-pSpA which is led by our group, have indicated a correlation between IBD disease activity and active large joint arthritis but no association with extent of joint involvement.[7] Consequently, we do not endorse utilization of Orchard criteria.

The rheumatology literature provides recommendations for SpA that could potentially be used in patients with IBD-SpA.[8–12] The most frequently utilized is the Assessment of Spondyloarthritis (ASAS) International Society criteria, which has good sensitivity (79.5%) and specificity (83.3%) for SpA.[3,8,12] Patients must have arthritis, enthesitis (pain and swelling where tendon attaches to bone) or sausage-like swelling of the entire finger or toe (dactylitis) and some

combination of SpA features including psoriasis, IBD, positive human leukocyte antigen (HLA)-B27, preceding infection, uveitis, and/or a family history of inflammatory back pain (IBP) or SpA.[12] These criteria are endorsed by European Crohn's and Colitis Organization (ECCO) guidelines.[6] However, only 2.3% of the patients in which use of this instrument was reported had IBD-pSpA, which to date limits validity in an IBD population.[12]

Given the low percentage of IBD-pSpA included in these criteria, two separate modified Delphi consensus panels were conducted.[13,14] The CHASE criteria, developed for clinical practice, specified that patients can be diagnosed based on 1) joint pain + swollen/tender joints on exam or 2) morning stiffness + joint pain + swollen/tender joints or 3) swollen/tender joints on exam with exclusion of other etiologies. While CHASE panelists agreed that rheumatologists are ideally trained for diagnosis IBD-pSpA, it was acknowledged that IBD providers may be capable of applying these criteria, especially given practical limitations of timely follow-up with rheumatology.[13] The International Organization for the Study of IBD (IOIBD) criteria, developed for clinical trials, suggested that diagnosis should rely on rheumatological expertise, which remains widely regarded as the gold standard across the literature.[14]

Patient history and exam: No constellation of symptoms and physical exam findings essential to diagnosis of IBD-pSpA have been conclusively established.[3] However, symptoms most commonly reported in the literature include joint pain manifesting with swollen/tender joints, morning stiffness (>1 hour), and dactylitis, which may interfere with performing everyday activities.[3] Personal or family history of arthritis, enthesitis, or dactylitis are frequently reported.[3]

Symptoms suggestive of other etiologies include report of widespread pain (suggestive of fibromyalgia or other chronic pain syndromes), history of recent injury (suggestive of a mechanical etiology), recent infection (suggestive of reactive arthritis or hepatitis related), recent tick bite or viral exposures (suggestive of Lyme arthritis or post viral syndromes), or limitation and pain with joint movement (suggestive of osteoarthritis).

There is significant heterogeneity and limitations to currently available screening tools for SpA.[15] Proposed screening tools for pSpA include the 14-item IBD identification of SpA questionnaire and the six-item Detection of Arthritis in IBD questionnaire, among others.[16–20]

Of note, there is no patient-reported outcome (PRO) instrument specific for IBD-pSpA. Early literature suggests that some validated metrics for axSpA including Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Axial Spondyloarthritis Disease Activity Score (ASDAS) may be of benefit in IBD-pSpA.[21] Other potential parameters of interest include patient global assessment of pSpA activity as well as patient report of peripheral pain, swelling, and morning stiffness.[21]

Physical examination is widely recommended, though findings go unreported in ~20% of studies.[3] The most commonly reported findings include enthesitis, dactylitis, or swollen/tender joints.[3] More subtle findings of enthesitis may require advanced imaging for detection. When physical examination for enthesitis is compared to imaging as a reference standard, sensitivity is 20-58% while specificity exceeds 80%.[22] It is important to note physical examination findings that may be suggestive of alternative diagnoses including a completely normal physical exam

(suggestive of arthralgia), skin/nail changes (suggestive of psoriatic arthritis), small joint destruction (suggestive of rheumatoid arthritis), an exquisitely red/tender joint with fever (suggestive of a septic joint) or the presence of a tophus (pathognomonic for gout).

Laboratory Data: There is no biomarker specific for diagnosis of IBD-pSpA. Data is insufficient to endorse use of any laboratory value, including HLA-B27, erythrocyte sedimentation rate (ESR), or C-reactive protein (CRP).[3] HLA-B27 has not been shown to be consistently associated with IBD-pSpA, however, can provide clues to axial involvement in the correct clinical context. ESR/CRP are non-specific and may be elevated secondary to active luminal IBD.[3] Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-CCP) are not expected to be positive in IBD-pSpA but may be ordered if there is concern for other seropositive arthropathies such as rheumatoid arthritis in an IBD patient.

Imaging: Data is currently insufficient to endorse any imaging modality for diagnosis. Few studies have assessed joint imaging in IBD-pSpA and most have significant limitations, such as inadequate patient numbers or lack of longitudinal follow-up.[3] X-ray examination can be a helpful starting point for evaluation of any joint problem, however, in IBD-pSpA may be best relied upon for demonstration of other pathology (e.g. osteoarthritis with findings such as joint space narrowing and/or osteophytes) as definitive findings of SpA are often not seen.[3] Magnetic resonance imaging (MRI) has a known role in diagnosis of other spondyloarthropathies, but only two studies with small patient numbers have evaluated MRI as a diagnostic tool for IBD-pSpA.[23–25] Given costs as well as limited data, MRI cannot be endorsed as a routine diagnostic modality.[3] Ultrasound as a screening and diagnostic tool is of interest given feasibility and

known role in diagnosis of other spondyloarthropathies.[26] Thirteen studies have examined peripheral joint ultrasound in IBD-pSpA either as a screening or diagnostic tool, with reliability of the most commonly reported abnormal features (entheseal thickening, enthosphytes) unknown.[3,27]

Summary of Recommended Diagnostic Approach: An evidence-based approach to diagnosis of IBD-pSpA is lacking (Table 2). We recommend a high degree of vigilance for the presence of IBD-pSpA given high prevalence. Providers should take a history encompassing questions regarding joint pain manifesting with swollen/tender joints, morning stiffness (>1 hour), dactylitis, and impact on performing everyday activities. They should perform a physical examination assessing any symptomatic joints for swelling/tenderness (along with the presence of other findings such as joint deformity suggestive of alternative diagnoses). European Alliance of Associations for Rheumatology-ASAS, American College of Rheumatology, CHASE, and IOIBD recommendations can be used to facilitate diagnosis. In patients with symptoms or examination findings concerning for an inflammatory joint process, we recommend rheumatology referral. Rheumatology referral should also be pursued in cases of diagnostic uncertainty. There is insufficient evidence to recommend gastroenterologists routinely order HLA-B27, ESR, or CRP to assist in diagnosis of IBD-pSpA, however this testing may be considered depending on the clinical context. The rheumatologist may also order this testing to facilitate their clinical decision making. The literature is insufficient to recommend routine use of any imaging modality, though ultrasound does show promise (Figure 1). While the gastroenterologist may order imaging during a clinic visit, given the limited available literature and limited experience with routine musculoskeletal imaging deferring to the rheumatologist regarding need for imaging and type of imaging is appropriate.

Axial SpA

Classification and consensus criteria: There are several criteria for classification and/or diagnosis of IBD-axSpA (Table 1). The ASAS criteria for axSpA indicate diagnosis should be made based on back pain ≥3 months in patients <45 with sacroiliitis on imaging plus ≥1 SpA feature or positive HLA-B27 and ≥2 SpA features.[28] SpA features include IBP, arthritis, heel enthesitis, uveitis, dactylitis, psoriasis, response to non-steroidal anti-inflammatory agents (NSAIDs), family history of SpA, positive HLA-B27, elevated CRP, and IBD.[28] As for pSpA, the rheumatology classification criteria for axSpA were not designed specifically for IBD patients, with only 3.8% of patients in which the instrument was reported diagnosed with IBD.[28]

Given this limitation, criteria for diagnosis of axSpA in IBD patients were developed via modified Delphi consensus panels for clinical practice (CHASE) and clinical trials (IOIBD).[13,14] According to CHASE criteria, IBD-axSpA should be diagnosed by rheumatology.[13] Patients should meet ASAS criteria or have IBP and consistent MRI findings.[13] According to IOIBD criteria, IBD-axSpA can be diagnosed via rheumatology expertise or in IBD patients with IBP/axial pain plus typical MRI findings.[14]

Patient history and exam: IBD patients should be asked about back pain . If back pain is present, IBD providers can deploy IBP criteria developed by rheumatologists (age at onset <40, insidious onset, improvement with exercise, no improvement with rest, and pain at night that improves upon getting up) to guide decision making.[29,30] Fulfilling at least four of these criteria has a high sensitivity (77%) and specificity (79.6%) for SpA.[29,30] Patients who do not meet criteria for IBP are more likely to have an alternative etiology for pain, such as a mechanical back pain. In

patients with a history of steroid exposure, it is also important to consider osteoporosis and compression fractures as potential etiologies of joint pain.

A physical examination is recommended but cannot be used in isolation. In patients in whom the diagnosis is suspected, expedited rheumatology evaluation is recommended.

While there is no PRO specific to IBD-axSpA, there are a number of validated metrics for axSpA (without IBD), including BASDAI and ASDAS.

Laboratory Data: Unlike for IBD-pSpA, in axSpA there may be utility in obtaining HLA-B27.[28] However, HLA-B27 is less likely to be positive in IBD patients, and we recommend deferring ordering this to the rheumatologist, who can better determine if it is necessary through a higher pre-test probability evaluation.[31] CRP can be ordered by the IBD provider but must be interpreted in context given IBD itself may elevate CRP.

Imaging: There is a known role for imaging in diagnosis of axSpA, though absence of sacroiliitis does not exclude the diagnosis. X-ray examination can be used for screening though may miss subtle findings that would be identified on cross-sectional imaging. Assessment of sacroiliac joints on either computed tomography (CT) enterography or MR enterography, which are obtained routinely as part of standard of care in IBD patients, may be helpful in identifying sacroiliitis. However, these changes can be subtle, and a request that a musculoskeletal radiologist render an opinion may be of benefit. Dedicated imaging of the sacroiliac joints may still be required for definitive diagnosis.

Summary of Recommended Diagnostic Approach: IBD providers should maintain a high level of suspicion for IBD-axSpA. Though less prevalent than IBD-pSpA, IBD-axSpA can be progressive and lead to joint damage if not identified early. IBD providers should screen for IBP, and patients who screen positive for IBP and/or patients with sacroiliitis found on routine IBD imaging should be promptly referred to rheumatology for diagnosis (Table 2). Given need for rheumatology co-management, we do not recommend the gastroenterologist routinely order screening lab work (HLA-B27) or order imaging prior to the first rheumatology consult. Instead, we advise deferring to rheumatology regarding the optimal testing to pursue (Figure 1).

Of note, some patients will have a mixed axial and peripheral arthritis phenotype. In these patients, the strategies outlined for both IBD-pSpA and IBD-axSpA should be applied.

MANAGEMENT

IBD-pSpA

The data surrounding specific IBD therapies in IBD-pSpA is limited and mostly extrapolated. Thus, further research is needed to establish an evidence-based approach in this population. However, we recommend beginning with objective assessment of luminal IBD disease activity through a combination of clinical symptoms, biomarkers such as fecal calprotectin, endoscopic evaluation, and intestinal ultrasound . If there is evidence of luminal activity, escalation of therapy with assessment of luminal and joint response should be pursued. Available therapeutic options are outlined in detail below.

If there is no evidence of luminal activity, disease modifying therapies to treat joint symptoms or a change in IBD therapy can be considered (Figure 2, Table 3). Decision making must be individualized based on the clinical scenario and should be made in collaboration with rheumatology. For example, in patients with luminal disease that has been challenging to treat, adjunctive therapy may be preferable while in patients with severe joint symptoms change to an IBD therapy that has known efficacy in SpA may be preferable.

Joint response can be assessed based on patient report of symptoms as well as provider assessment of joint disease on physical examination.[13,14] Close collaboration with rheumatology for joint assessment is again essential. Though limited, there are some data to suggest that ESR/CRP may assist in longitudinal evaluation of IBD-pSpA and assessment of therapeutic response.[32–34] When available, A PRO developed and validated specifically for IBD-pSpA patients would also be of benefit in assessing joint response.[21]

5-Aminosalicylates (5-ASA): A Cochrane systematic review (SR) designed to evaluate efficacy of sulfasalazine in patients with ankylosing spondylitis (IBD and pSpA patients were included) recommends against its use.[35] However, given a multi-center randomized controlled trial (RCT) demonstrating treatment response (based on patient and physician assessment of peripheral joint symptoms/swelling) in sulfasalazine vs placebo (59% vs 42.7%, p=0.0007), sulfasalazine is a recommended IBD-pSpA treatment.[6,36] Sulfasalazine can be administered as monotherapy in patients with mild to moderate ulcerative colitis (UC) or as adjunctive therapy in patients with joint pain despite luminal remission.[37]

Immunomodulators: Another Cochrane SR designed to evaluate efficacy of methotrexate in patients with ankylosing spondylitis did not find improvement in pSpA in subgroup analyses.[38] However, based on a small study of patients with IBD-pSpA (n=18) with improvement in ESR/CRP, functional status, and disease activity (based on patient symptoms and physical exam findings), methotrexate is a recommended IBD-pSpA therapy.[6,39]

Advanced IBD therapies: Though high-quality data in the form of dedicated RCTs is unavailable,

anti-tumor necrosis factor (TNF) agents have the most evidence to support their use in treatment of IBD-pSpA. In the Swiss IBD cohort, there was a 73% response rate, defined as physician global assessment of clinical improvement, for patients with arthritis (n=158) treated with anti-TNF therapy.[40] In a SR looking at efficacy of anti-TNF agents, reduction in prevalence of pSpA from 8.7>2.1% at week 20 (n=945, $p<0.001$) and 58.1>12.5% at 6 months (n=24, $p<0.01$) was seen in two open-label studies.[41–43] We thus recommend anti-TNF therapy first line for patients with IBD-pSpA.

Both janus kinase inhibitors (JAKi) approved for IBD have been approved for other inflammatory joint diseases including psoriatic arthritis (PsA), rheumatoid arthritis, and axSpA.[44–49] In addition, post hoc analyses of maintenance trials demonstrate resolution of IBD-pSpA and IBD-axSpA by week 52 in a statistically significant proportion of patients on upadicitinib (66.7% 30 mg, 38.5% 15 mg, vs 22.2% placebo, p=0.010) and improvement in pSpA (based on patient report) in a higher proportion of patients on tofacitinib (33.3% 10 mg BID, 16.7% 5 mg BID, vs 18.2% placebo, p value not provided).[50,51]

Data regarding efficacy of α4β7 agents in IBD-pSpA is conflicting. A post-hoc analysis of the GEMINI trial for vedolizumab as induction and maintenance therapy for IBD found reduced likelihood of new or worsening arthritis in patients with Crohn's disease (CD) (hazard ratio 0.63; 95% confidence interval (CI), 0.44-0.89) and no increased incidence of arthritis in patients with UC.[52] Analysis of the MarketScan database suggested those with CD had an increased likelihood of developing arthritis on vedolizumab (adjusted incident ratio 1.45; 95% CI 1.15-1.84) but those with UC did not.[53] A post-hoc analysis of the French observatory on effectiveness and safety of vedolizumab in patients with IBD found that ~14% of patients developed incident joint symptoms (predominantly arthralgia though also arthritis).[54]

The data surrounding interleukin-12/23 (IL-12/23) and IL-23 agents is insufficient. Studies in patients receiving ustekinumab noted improvement in arthralgia and PsA as well as lower rates of incident arthralgia in comparison to vedolizumab, however larger and controlled studies evaluating response specifically in IBD-pSpA are not available.[55,56] One small prospective study (28 patients with pSpA received ustekinumab) noted no significant improvement in systemic joint symptoms using validated SpA disease activity indices.[57] Risankizumab is approved for PsA suggesting a possible role in treating joint inflammation, but there is insufficient data regarding efficacy in IBD-pSpA.[58]

We therefore recommend JAKi and α4β7 agents as second line therapies in patients with IBD-pSpA. The role of IL-12/23 and IL-23 agents in IBD-pSpA patients represents an unmet need in the literature that warrants further exploration. There is not yet sufficient data regarding efficacy of sphingosine-1 phosphate receptor modulators (S1P) and so at this time these are not recommended.

NSAIDs: NSAIDs effectively treat SpA symptoms but use in IBD has historically raised concerns for triggering flares. Given emerging data suggesting no risk of flare in UC and only potential risk in CD, guidelines support short courses of gut-selective NSAIDs (specifically cyclooxygenase-2 inhibitors such as celecoxib).[6] We recommend consideration of use for up to two weeks in patients with significant joint symptoms but well-controlled luminal IBD while pursuing alternative maintenance strategies.

Steroids: Steroids are also efficacious in treating joint pain but due to side effect profile should be used sparingly while pursuing alternative maintenance strategies.

Follow-up

Patients with active joint pain receiving treatment should be seen at least every 3 months (and more frequently if needed) until symptoms improve or resolve.[13,14]

IBD-axSpA

There are no RCTs dedicated specifically to IBD-axSpA. However, we can extrapolate based on trials designed for IBD and axSpA. Anti-TNF agents and JAKi have been approved for IBD and axSpA and are thus recommended first line for IBD-axSpA (Figure 2, Table 3).[44,47,59,60] Data has not supported a role for sulfasalazine, immunomodulators, or other advanced IBD therapies (α4β7, IL-23, IL-12/23, S1P agents) for treatment of axSpA, and we do not endorse their use.[6] NSAIDs and steroids can be used for symptomatic relief as already outlined for IBD-pSpA but neither are disease modifying.

All treatment decisions should be made in multi-disciplinary fashion via collaboration between IBD specialist and rheumatologist. Ideally, either an anti-TNF agent or JAKi should be initiated with assessment of luminal response by the IBD provider and axSpA response by the rheumatologist. If response is seen luminally but not axially, alternative agents approved for axSpA may need to be considered in conjunction with use of an IBD advanced therapy. Of note, use of etanercept or IL-17 inhibitors for axSpA is not recommended given risk of IBD exacerbation. Similarly, if response is seen axially but not luminally, alternative agents approved for IBD may need to be considered in conjunction with use of axSpA advanced therapy. ECCO guidelines recommend caution with vedolizumab in SpA given concern for paradoxical arthritis activity.[6] Validated axial SpA metrics (BASDAI, ASDAS) can also be incorporated to assess treatment response over time.

Follow-up

Patients should be seen at least every 3 months (and more frequently if needed) until symptoms improve or resolve.[13,14]

Patients with IBD-mSpA should be treated using agents appropriate for management of IBD-axSpA.

CONCLUSION AND FUTURE DIRECTIONS

IBD-SpA is commonly encountered in clinical practice and yet there is limited guidance available regarding diagnosis and management. For IBD-pSpA, a diagnostic approach incorporating classification criteria, patient symptoms and physical exam with reliance on rheumatology expertise should be employed until more evidence-based approaches are established. For diagnosis of IBD-axSpA, we recommend early rheumatology referral and reliance on classification criteria along with a combination of symptoms, laboratory data, and imaging to make the diagnosis.

It is important to note that the lack of clarity regarding diagnostic approaches is a limitation to this review and a major barrier to progress in the field. To address this unmet need, our group is currently leading a multi-disciplinary RAND panel composed of gastroenterologists, rheumatologists, radiologists, and patient advocates with the goal of standardizing approaches to diagnosis of IBD-pSpA, thereby reducing delays in care. In parallel, we are leading a study exploring the role of ultrasound as a screening and diagnostic strategy for IBD-pSpA with the aim of providing an objective and reproducible tool for diagnosis of IBD-pSpA.

With regards to therapeutic management, for IBD-pSpA we recommend starting with assessment of luminal IBD activity along with referral to rheumatology. Anti-TNF agents have the most robust data to support their efficacy in treatment of joint symptoms followed by JAKi. There is limited data to support use of IL-23 and IL-12/23 agents, mixed data to support use of vedolizumab, and insufficient data to make a recommendation regarding use of S1P agents.

Sulfasalazine and methotrexate may also be considered. For axSpA, co-management with rheumatology is required. We recommend use of anti-TNF agents and JAKi.

Limited data surrounding therapeutics in IBD-SpA represents another unmet need in this patient population. Our group is currently conducting a SR to better understand efficacy of available therapies for IBD-pSpA. Via the CHASE registry, we are also collecting prospective data regarding therapeutic response of IBD-pSpA to standard of care treatment over time across multiple centers in the US, with the goal of improving patient outcomes by providing higher quality data regarding efficacy of available treatments. Finally, there is not yet a PRO solely dedicated to IBD-pSpA, which represents a major limitation to assessment of treatment response. For this reason, our group is developing a PRO for IBD-pSpA to close this gap in the literature and improve clinical outcomes.

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Figure 1: Diagnostic Algorithm for IBD-SpA

IBD: inflammatory bowel disease; SpA: spondyloarthritis; pSpA: peripheral SpA; axSpA: axial SpA; ASAS: Assessment of Spondyloarthritis; MRI: magnetic resonance imaging

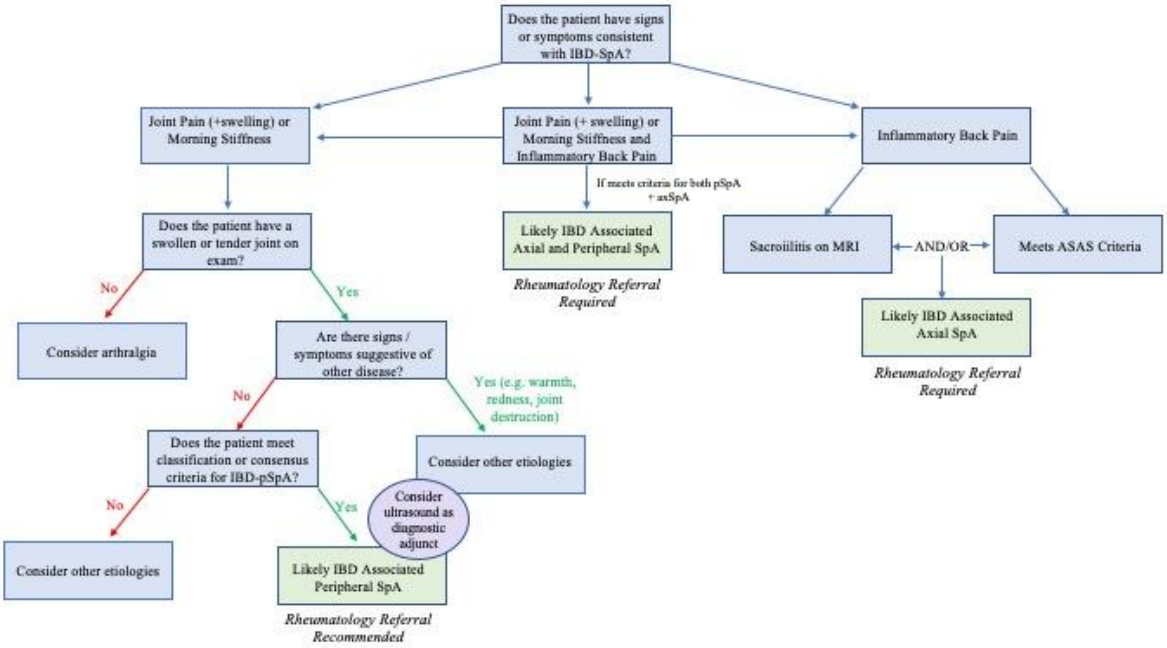


Figure 2: Treatment Algorithm for IBD-SpA

IBD: inflammatory bowel disease; SpA: spondyloarthritis; anti-TNF: anti-tumor necrosis factor; JAK inhibitor: janus kinase inhibitor, IL: interleukin

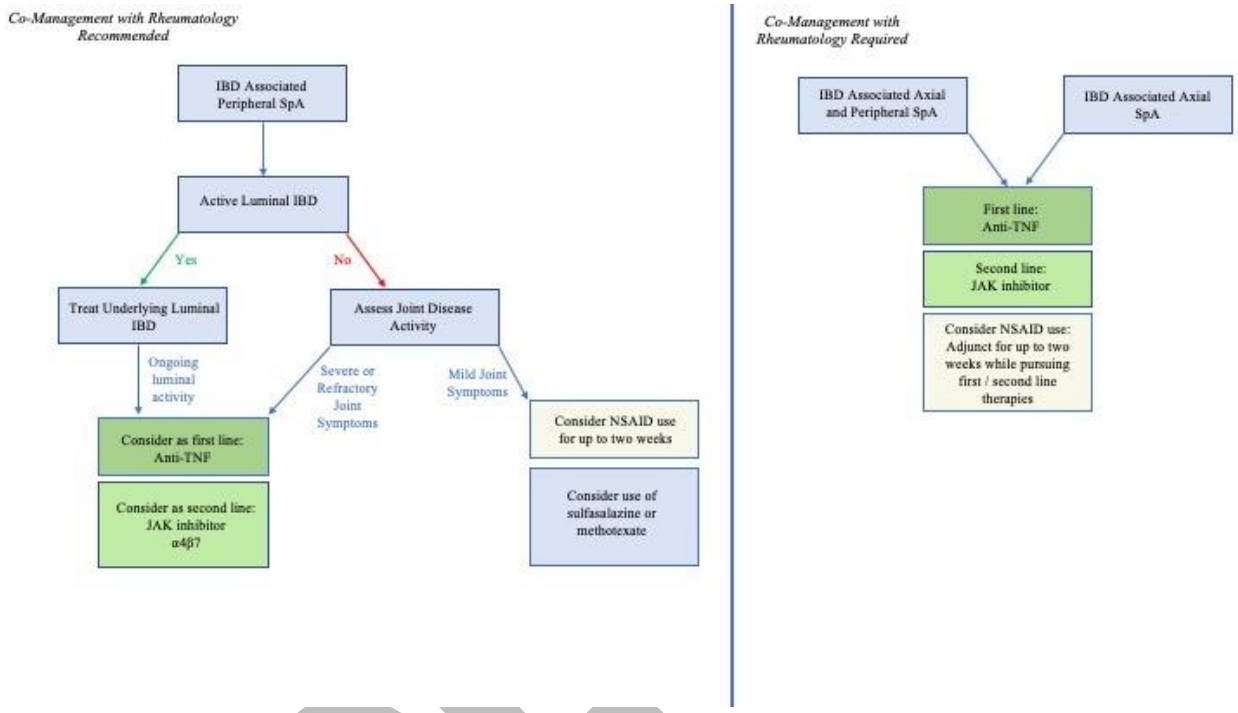


Table 1: Available Clinical Definitions

Clinical Definitions	IBD-pSpA		IBD-axSpA
Orchard Criteria	Type I	Type II	N/A
	<5 joints Asymmetrical Large joints Active Luminal IBD	≥5 joints Symmetrical Small Joints Inactive Luminal IBD	
CHASE Criteria	Joint pain + swollen/tender joints on exam OR Morning stiffness + joint pain + swollen/tender joints OR Swollen/tender joints on exam with the exclusion of other etiologies		Patient who meets ASAS classification criteria for arthritis as per rheumatologist OR Patients with IBD, inflammatory back pain, and consistent MRI findings as per rheumatologist
IOIBD Criteria	Rheumatologist expertise		Rheumatologist expertise OR Inflammatory back or axial pain plus typical MRI in patients with IBD
ASAS Criteria	Arthritis OR Enthesitis OR Dactylitis + ≥1 of: psoriasis, IBD, preceding infection, HLA-B27, uveitis, sacroiilitis on imaging (radiographs or MRI) OR ≥ 2 of the remaining: arthritis, enthesitis, dactylitis, inflammatory back pain in the past, positive family history for SpA		Sacroiilitis on imaging plus ≥1 SpA feature OR HLA-B27 plus ≥2 other SpA features SpA features: inflammatory back pain, arthritis, enthesitis (heel), uveitis, dactylitis, psoriasis, Crohn's disease/ulcerative colitis, good response to non-steroidal anti-inflammatory agents, family history for SpA, HLA-B27, elevated CRP

IBD: inflammatory bowel disease; SpA: spondyloarthritis; pSpA: peripheral SpA; axSpA: axial SpA; CHASE: Cohort for Healing Arthritis, Skin and Eye Extra-Intestinal Manifestations; ASAS: Assessment of Spondyloarthritis; MRI: magnetic resonance imaging (MRI); IOIBD: International Organization for IBD; HLA-B27: human leukocyte antigen-B27

Table 2: Summary of Role of Diagnostic Strategies for IBD-pSpA

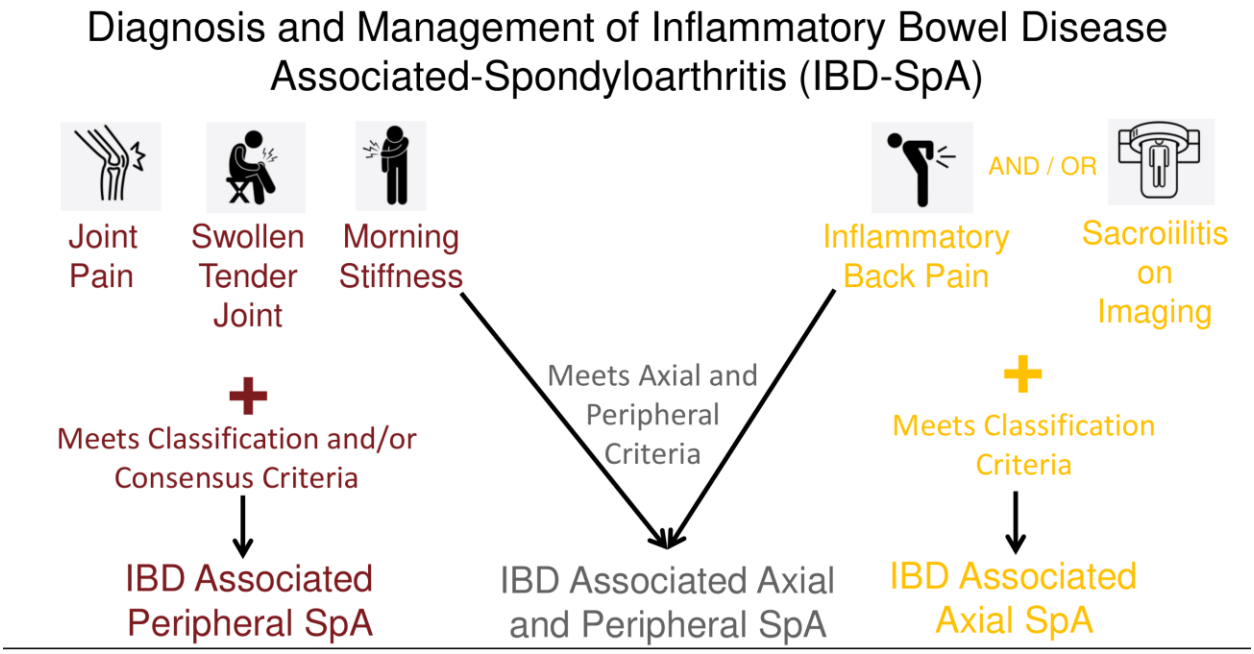
Modality	IBD-pSpA	IBD-axSpA
Classification Criteria	Orchard Criteria: For use in clinical practice with caution as no longer endorsed by guidelines ASAS: For use in clinical practice and clinical trials CHASE: For use in clinical practice IOIBD: For use in clinical trials	ASAS: For use in clinical practice and clinical trials CHASE: For use in clinical practice IOIBD: For use in clinical trials
Key Patient Symptoms	Joint pain (along with joint swelling) and/or morning stiffness	Inflammatory Back Pain
Key Physical Examination Findings	Swollen or tender joint, dactylitis, pain at entheses	Physical examination may be normal, assess for impaired spinal mobility and postural abnormalities
Laboratory Findings	No available biomarker at this time	+ HLA-B27, Elevated CRP (though non-specific in the setting of IBD)
Imaging	Insufficient data to recommend imaging at this time	Recommended
Imaging Findings	X-ray examination: likely normal CT: not routinely recommended MRI: not routinely recommended, may show joint space and / or entheseal abnormalities US: not routinely recommended, may show joint space and / or entheseal abnormalities	X-ray examination: may show sacroiilitis CT: may show sacroiilitis MRI (preferred): may show sacroiilitis US: not recommended at this time

IBD: inflammatory bowel disease; SpA: spondyloarthritis; pSpA: peripheral SpA; axSpA: axial SpA; ASAS: Assessment of Spondyloarthritis; CHASE: Cohort for Healing Arthritis, Skin and Eye Extra-Intestinal Manifestations; IOIBD: International Organization for IBD; HLA-B27: human leukocyte antigen-B27; CRP (C-reactive protein); CT: computed tomography; MRI: magnetic resonance imaging; US: ultrasound

Table 3: Selecting a Therapy for IBD Associated Arthritis

Medication	IBD-pSpA	IBD-axSpA
Non-Steroidal Anti-Inflammatory	Yes for symptoms	Yes for symptoms
5-Aminosalicylate	Yes	No
Methotrexate	Yes	No
Azathioprine / 6-mercaptopurine	No unless to treat underlying IBD	No
Anti-tumor necrosis factor	Yes	Yes
α4β7	Mixed data	No
Interleukin-12/23	Unmet Need, Limited Data	No
Interleukin-23	Unmet Need	No
Janus kinase inhibitor	Yes	Yes
Sphingosine-1 phosphate receptor modulator	Unknown	No

IBD: inflammatory bowel disease; SpA: spondyloarthritis; pSpA: peripheral SpA; axSpA: axial SpA



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