GHAPP E-Newsletter Series

The Current State of and Future Directions in Inflammatory Bowel Disease

Project ID: 5838

Target Audience

Nurse practitioners and physician assistants involved in the management of patients with chronic liver disease.

Educational Objectives:

Upon completion of this activity, participants will be able to:

- Describe the symptoms, diagnosis and treatment of inflammatory bowel disease (IBD)
- Discuss the impact of IBD on patient quality of life
- Identify future directions in the management of IBD
- Analyze the role of the APP in IBD management

ANCC Accreditation

Annenberg Center for Health Sciences is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

A maximum of 1.0 contact hours may be earned for successful completion of this activity.

Physician Assistant Statement

This activity has been reviewed by the AAPA Review Panel and is compliant with AAPA CME Criteria. This activity is designated for 1 AAPA Category 1 CME credits. Approval is valid from 7/31/2021 to 7/31/2022. PAs should only claim credit commensurate with the extent of their participation. AAPA reference number: CME-202397.

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Inflammatory bowel disease (IBD) refers to a group of chronic intestinal disorders characterized by alternating periods of remission and relapse. Crohn's disease (CD) and ulcerative colitis (UC) are the main types of IBD. Ulcerative colitis is limited to the colon while Crohn's disease can occur anywhere between the mouth and the anus. In Crohn's disease, there are healthy parts of the intestine mixed in between inflamed areas. Ulcerative colitis, on the other hand, is continuous inflammation of the colon.

Ulcerative Colitis Compared to Crohn's Disease

In 2015, an estimated 1.3% of US adults (3 million) reported being diagnosed with IBD (either CD or UC),[1] which is a significant increase from the 1999 estimate (0.9%, 2 million).[2] Patients with IBD commonly experience abdominal pain, diarrhea, fever and rectal bleeding, and frequent complications including abscesses, fistulas, and stenosis.[3] IBD represents a life-long disease which might require daily medication, frequent doctor's appointments, and possible hospitalizations or surgery in a considerable number of patients.[4] Understandably, quality of life (QoL) for individuals with IBD has been demonstrated to be poorer than for healthy individuals, including both adults and children.[5]

Pharmacological therapy includes both conventional and biologic treatments.[6] As the understanding of IBD continues to evolve, there are several newer classes of biologics targeting alternative pathways with lower immunogenicity rates and favorable safety profiles. Current and emerging IBD treatments are aimed not only at relieving symptoms and reducing complications but also at improving patient's quality of life.[6] Caring for a patients "global health" includes considering the psychological, social and emotional aspects of the disease.[7] Data demonstrates that, although 84% of IBD patients trust their gastroenterologist, only 66% of them discussed IBD impact on health-related (HR)QoL during appointments.[5]

Rayhorn and colleagues conducted an internet-based survey of advanced practice providers (APPs), who specialize in gastroenterology, in order to define their role in the care of IBD. Respondents spent the majority of their time (86%) in direct patient care, and the roles highlighted in the results indicate that they are significantly involved in the care of complex IBD patients. APPs are positioned to enhance the diagnosis and management of IBD, including effects on HRQoL.[8]

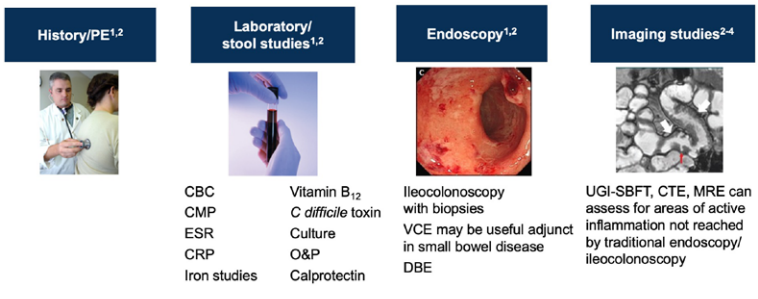
APP Roles in the Care of IBD Patients

Role in Practice	Total (%) (n=99)
Follow-up visits	100
Prescription refills	97
Patient education	97
Discussion with patients about therapeutic options	95
Instruction on how to administer medication	91
Lab monitoring	91
Prescription initiation	90

The Diagnosis and Clinical Features of IBD

The diagnosis of IBD is based on a combination of clinical, endoscopic and histopathologic findings.

IBD Diagnosis Is Based on Combination of Clinical, Endoscopic, and Histopathologic Findings



1. Sands BE. *Gastroenterology*. 2004;126:1518-1532; 2. Lichtenstein GR et al. *Am J Gastroenterol*. 2018;113:481-517; 3. Kilcoyne A et al. *World J Gastroenterol*. 2016;22(3):917-932; 4. Bruining DH et al. *Radiology*. 2018;286(3):776-799.

When a patient presents with symptoms suggestive of IBD, the clinician's task is, first, to perform a differential diagnosis to establish if the disease is, in fact, IBD.[9] For instance, IBD can be confused for

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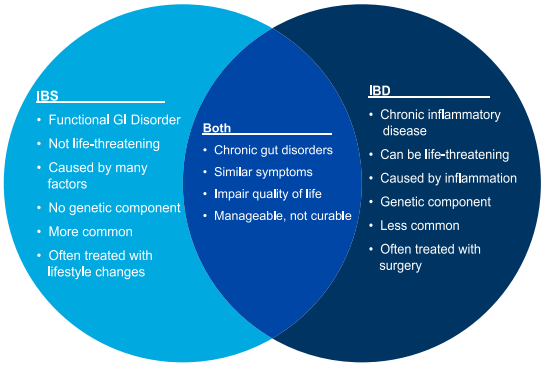
irritable bowel syndrome (IBS), because both conditions are gut-related and symptoms may overlap, but there are some distinct differences. Pooled data from 13 studies involving 1,703 patients indicated that the prevalence of symptoms compatible with IBS in patients with IBD is ~40%.[10] Unlike IBD, IBS is not typically associated with rectal bleeding, systemic signs of illness (eg, weight loss), laboratory evidence of inflammation (eg, increased CRP, ESR, fecal calprotectin) and abnormal findings on colonoscopy.[11]

A Comparison of IBS and IBD



Available at: https://www.kansashealthsystem.com/news-room/blog/0001/01/ibs-ibd-difference. Accessed June 15, 2020.

An additional key component of the diagnosis of IBD is to differentiate between UC and CD.[9] Although the presenting symptoms of IBD may suggest a particular diagnosis, they are not often definitive.[9] Endoscopy is used to make an initial diagnosis of IBD and distinguish between UC and CD.

Key Clinical Features of IBD

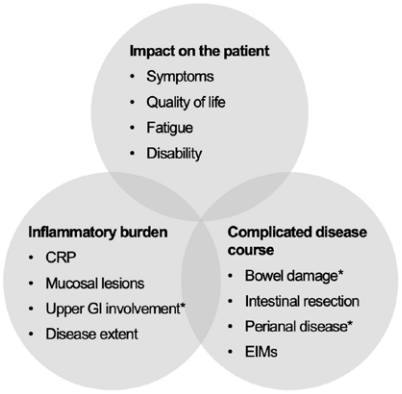
Clinical features	Ulcerative colitis	Crohn's disease
Diarrhea[1]	Very common	Fairly common
Fever[1]	Fairly common	Common
Abdominal pain[1]	Varies	Common
Rectal bleeding[1]	Very common	Fairly common
Weight loss[1]	Fairly common	Common
Passage of mucus or pus[2]	Common	Rare
Perianal disease[1]	Absent	Fairly common
Fistulas[2]	Absent	Common
Growth failure in children/adolescents[1]	Occasional	Common

1. Podolsky DK. *N Engl J Med*. 2002;347:417-429; 2. Baumgart DC, Sandborn WJ. *Lancet*. 2007;369:1641-1657.

Impact of IBD on Patient Quality of Life

When discussing disease severity in IBD, it is important to consider the impact of disease on the patient, disease burden, and disease course. As discussed, patient QoL is significantly impacted from IBD.[12] In fact, IBD patients experience moderate functional impairment more in the social and psychological than in the physical dimensions.[13]

Factors that Determine Disease Severity in IBD



The following has been found with regard to IBD and QoL:

- Patients with IBD are impacted in terms of physical functioning, social and emotional well-being and ability to go to work/school[14]
- Diminished QoL can be attributed to, in part, by the symptoms associated with IBD. In addition, about 25% of the patients also suffer from abscesses, fistulas, and stenosis.
- Disease progression may further reduce patients' quality of life and increase their disability
- Patients with IBD have concerns about having surgery, degree of energy, and body image issues, such as having an ostomy bag, which affect QoL.[13]
- One study demonstrated that quality of life is associated with active disease, anemia, presence of extraintestinal manifestations, and Crohn phenotype.[15]
- Food-related quality of life (FRQoL), which evaluates the impact of diet, eating behaviors, and food-related anxiety on a person's quality of life, is also impacted in IBD patients.[16]
- In a study by Graff and colleagues, participants with either active or inactive disease had suboptimal general QoL, indicating that there is a continued impact on QOL by the disease, even when it is inactive.[17]

Future Directions in the Management of IBD

Current IBD treatment is aimed not only at relieving symptoms and reducing complications but also at improving patient quality of life. Pharmacological therapy in IBD depends on disease severity and location and includes both conventional therapies (eg, aminosalicylates, corticosteroids, and immunosuppressive agents) and biologic treatments targeting a specific inflammatory mediator instead of exerting a larger immune suppression (eg, anti-TNFs).[6] The American College of

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Gastroenterology has published guidelines on the use of these drugs for managing UC[14] and CD[6].

Although biologics have greatly improved the management of IBD, many patients discontinue these therapies due to limited efficacy, adverse events and parenteral administration. Approximately 30% of patients are primarily unresponsive to anti-TNF and even among responders, up to 10% will lose their response to the drug every year.[18] Beyond TNF antagonists, several new biologics are either approved or in late-stage development. Emerging therapies target alternative pathways, have low immunogenicity rates and favorable safety profiles.[19, 20]

New and Emerging Therapies in IBD

Class	Description	Approved Drugs and Drugs in Development for IBD
Orally Administered Anti-TNFs	Orally administered anti-TNFs may offer an alternative to both SC and IV infusions of traditional anti- TNFs in UC, with lower immunogenicity and systemic side effects	AVX-470
Anti-Adhesion Antibodies	Anti-adhesion antibodies selectively target integrins controlling cell homing to the intestine, which leads to reduction of inflammatory infiltration to the gut in chronic intestinal inflammation	Vedolizumab (approved) Etrolizumab Abrilumab PF-00547659
IL-12/IL-23 inhibitors	These inhibitors prevent IL-12 and IL-23 from binding to the IL-12Rβ1 receptor chain of IL-12 and IL-23 receptor complexes on the surface of NK and T cells, neutralizing IL-12 and IL-23-mediated responses	Ustekinumab Risankizumab
JAK Inhibitors	Cytokines activate intracellular JAKs, which causes phosphorylation and activation of STAT proteins, regulating the expression of target genes. The JAK–STAT pathway is shown to be involved in the pathogenesis of IBD, and because JAKs are activated in pairs and in various combinations of cytokine receptors, JAK inhibition has the potential to block several inflammatory pathways concomitantly	Tofacitinib (approved) Filgotinib Ritlecitinib + brepocitinib
Sphingosine-1-phosphate receptor modulators	S1P modulators bind to the S1P receptor and induce its internalization and degradation, trapping lymphocytes within lymphoid tissue. This results in a reduction in the levels of circulating effector T cells and causes selective immunosuppression, without downregulating overall immune function	Ozanimod (approved)
Phosphodiesterase 4 inhibitors	PDE4 inhibition also leads to reduced TNFα messenger ribonucleic acid expression via transcriptional modulation of NF-κ-B and increased synthesis of IL-10, an anti-inflammatory cytokine, via activation of protein kinase A (PKA)	Apremilast

The most recent approval (May 2021) was for ozanimod, the first sphingosine 1-phosphate (S1P) receptor modulator, taken orally once-per-day for moderately-to-severely active UC. The approval is based on data from True North, a Phase 3 trial evaluating ozanimod as an induction and maintenance therapy versus placebo in adult patients with moderately to severely active UC. During induction at Week 10 (ozanimod N=429 versus placebo N=216) the trial met its primary endpoint of clinical remission (18% versus 6%, p<0.0001) as well as key secondary endpoints, including clinical response (48% versus 26%, p<0.0001), endoscopic improvement (27% versus 12%, p<0.0001) and endoscopic-histologic mucosal improvement (13% versus 4%, p<0.001) for ozanimod versus placebo, respectively. During maintenance at Week 52 (ozanimod N=230 versus placebo N=227) the trial met its primary endpoint of clinical remission (37% versus 19%, p<0.0001) as well as key secondary endpoints, including clinical response (60% versus 41%, p<0.0001), endoscopic improvement (46% versus 26%, p<0.001), corticosteroid-free clinical remission (32% versus 17%, p<0.001) and endoscopic-histologic mucosal improvement (30% versus 14%, p<0.001) for ozanimod versus placebo, respectively.

These newly-approved and emerging therapies are getting us closer to having drugs or drug combinations for all patients that are conveniently dosed (oral) and highly effective without infectious or malignant side-effect profiles. The field continues to evolve, with agents with unique mechanisms of action that inhibition inflammation (eg, inhibition of tumor progression locus 2 (TPL2) inhibition, interleukin-1 receptor-associated kinase 4 (IRAK4) and FimH-mediated inflammation) also being studied for use in IBD.

Conclusions: The Impact of These Data/Recommendations on How APPs Practice

[PLACEHOLDER]

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