STATEMENT

INTESTINAL RESEARCH

pISSN 1598-9100 • eISSN 2288-1956
https://doi.org/10.5217/ir.2023.00050
Intest Res 2024;22(3):213-249

Management of ulcerative colitis in Taiwan: consensus guideline of the Taiwan Society of Inflammatory Bowel Disease updated in 2023

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Received April 3, 2024. **Revised** April 25, 2024. **Accepted** April 29, 2024.
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Ulcerative colitis (UC) is a chronic inflammation of the gastrointestinal tract and is characterized by alternating periods of inflammation and remission. Although UC incidence is lower in Taiwan than in Western countries, its impact remains considerable, demanding updated guidelines for addressing local healthcare challenges and patient needs. The revised guidelines employ international standards and recent research, emphasizing practical implementation within the Taiwanese healthcare system. Since the inception of the guidelines in 2017, the Taiwan Society of Inflammatory Bowel Disease has acknowledged the need for ongoing revisions to incorporate emerging therapeutic options and evolving disease management practices. This updated guideline aims to align UC management with local contexts, ensuring comprehensive and context-specific recommendations, thereby raising the standard of care for UC patients in Taiwan. By adapting and optimizing international protocols for local relevance, these efforts seek to enhance health outcomes for patients with UC. **(Intest Res 2024;22:213-249)**

Key Words: Ulcerative colitis; Management; Guidelines; Consensus; Taiwan

INTRODUCTION

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) and immune-mediated disorder that initiates in the rectum and extends toward the proximal portions of the colon, leading to persistent inflammation and cycles of active disease and remission.[1] UC is less common in Asia than in Western countries, but its frequency has consistently increased in Taiwan.[2-7] The goals of UC treatment include initiating and sustaining remission, minimizing the likelihood of complications, and enhancing quality of life (QoL). The extent and severity of the disease, disease course over time, comorbidities, and patient preferences influence treatment selection.[8]

Guidelines for diagnosing and treating UC have been established in Europe, North America, and Asia-Pacific.[9-12] However, these guidelines may not fully align with clinical practices in Taiwan owing to variations in the distribution and behavior of the disease, the presence of endemic diseases, and disparities in insurance coverage for treatments. Taiwan's National Health Insurance (NHI), a compulsory social health insurance system implemented in 1995, currently covers over 99% of the Taiwanese population.[13] Under the NHI, IBD is categorized as a catastrophic illness, enabling UC patients to be reimbursed for treatments covered by the NHI without copayment. However, because of budget considerations, there is a limited period and mandatory drug holiday for advanced therapy.[14,15] Furthermore, in Taiwan, advanced therapy is initiated in patients with a Mayo score of 9, whereas in other countries, it is indicated in those with moderate to severe diseases (Mayo score >6).

Given the unique aspects of the medical environment in Taiwan and other countries, UC management guidelines specifically tailored to Taiwan's context are crucial. The Taiwan Society of Inflammatory Bowel Disease (TSIBD) established a steering committee that published the first edition of its diagnosis and treatment guidelines for IBD in 2017.[16] Given the recent emergence of novel treatment options and evolution of treat-to-target concepts for disease monitoring, the steering committee opted to update the guidelines. After comprehensively reviewing international guidelines and the latest literature, a consensus was reached and subsequently revised under Taiwan's practice scenario.

METHODS

TSIBD organized a steering committee to create expert consensus statements for diagnosing and treating UC, which were developed based on international guidelines and factors specific to Taiwan. The guidelines are recommendations only and should not replace clinical judgment. When making clinical decisions, healthcare professionals should consider individual patient factors and the facilities and treatments available in their institutions.

The steering committee comprised a panel of 30 experts, including gastroenterologists, surgeons, radiologists, and pathologists, who drafted recommendations for the clinical management of UC. They carefully reviewed available evidence and guidelines from organizations such as the European Crohn's and Colitis Organisation (ECCO) and the Asian Pacific Association of Gastroenterology. The entire expert panel held face-to-face meetings to discuss and modify the statements and evaluate the evidence for and against each one. The panel members indicated their agreement with the finalized statements as "strongly agree," "agree," or "disagree," with the strength of the recommendation reflected in their level of agreement. Consensus was achieved when at least 90% of the voting members indicated "strongly agree" or "agree."

https://doi.org/10.5217/ir.2023.00050 • Intest Res 2024;22(3):213-249

RESULTS

1. Epidemiology

Statement 1.1
The incidence and prevalence of UC in Taiwan are increasing, but this number is still underestimated. Level of agreement: Strongly agree, 76.7%; agree, 23.3%; disagree, 0.0%.

An analysis of the population-based Taiwan NHI Research Database (NHIRD)[17] showed that UC incidence and prevalence in Taiwan have consistently and significantly (both $P<0.0001$) increased over 3 periods: 2001–2005 (0.79 and 3.70 per 100,000 person-years, respectively), 2006–2010 (0.94 and 7.68 per 100,000 person-years, respectively), and 2011–2015 (0.79 and 11.36 per 100,000 person-years, respectively). The crude incidence of UC increased from 0.54 per 100,000 person-years in 2001 to 0.95 per 100,000 person-years in 2015.[17] Moreover, the crude prevalence of UC increased from 2.1 per 100,000 person-years in 2001 to 12.8 per 100,000 person-years in 2015.[17] Using more rigorous criteria in catastrophic illness registration, which includes clinical records, endoscopic images, and pathology results, instead of relying solely on clinical diagnostic data may lead to potential underestimations of incidence and prevalence. Another NHIRD-based epidemiological study found the prevalence of UC in Taiwan to be 12.4 per 100,000 persons in 2013.[7]

In Canada, one of the highest incidences of IBD is in Nova Scotia. Notably, the annual incidence of UC in this province declined from 21.4–16.7 per 100,000 person-years from 1996 to 2009.[18] In Europe, UC incidence varies among countries, ranging from 10.7–18.6 per 100,000 persons in Denmark between 1980 and 2013 and 11.67–21.47 per 100,000 persons in the Netherlands from 1991 to 2010.[19,20]

Two decades ago, unlike in Western countries, IBD was considered a rare condition in Asia. However, recent research has revealed a rapid IBD emergence in this region.[21] Crohn's disease (CD) incidence has increased faster than UC incidence in Asia, closing the gap between the number of prevalent CD and UC cases in the region.[21] The increasing IBD incidence in Taiwan and other Asian countries may be attributed to improved socioeconomic status, a Westernized diet, increased awareness of the disease, and enhanced accuracy in IBD diagnosis. Furthermore, endoscopic technology advancements, such as capsule endoscopy and deep enteroscopy, have enhanced the accuracy of IBD diagnosis.[17,21,22]

Statement 1.2
In Taiwan, similar to other Eastern Asian countries but in contrast to Western countries, UC is more common in men. Level of agreement: Strongly agree, 60.0%; agree, 40.0%; disagree, 0.0%.

An examination of NHIRD data showed a male predominance in IBD in Taiwan, particularly for CD compared to UC, throughout the 3 periods (2001–2005, 2006–2010, and 2011–2015). The overall male-to-female ratio was 1.62 for UC and 2.19 for CD.[17] Combined analysis of studies from Europe, North America, and Oceania revealed that the overall incidence of UC is not influenced by sex.[19,21] However, examining data from Western populations presents that males aged ≥45 years are at a higher risk for UC.[21,23] Similar to Taiwan, East Asia had a more balanced sex disparity for UC than for CD, with an overall male-to-female ratio of 1.58 in Guangdong Province, China; 1.30 in Korea; and 1.14 in Japan.[24-26] Genetic differences between Asian and Western populations may play a role, and the cultural preference for males in Asian societies may result in distinctions in breastfeeding practices, childhood antibiotic usage, and the subsequent development of IBD between male and female infants.[27,28]

Statement 1.3
In Taiwan, the prevalence of extraintestinal manifestations (EIMs) ranges from 2.8% to 26.6% in patients with UC. Level of agreement: Strongly agree, 40.0%; agree, 60.0%; disagree, 0.0%.

EIMs can precede the onset of gastrointestinal symptoms in approximately 25% of patients.[29] EIMs associated with UC affect the musculoskeletal, cutaneous, hepatobiliary, and ocular systems, with arthropathy being the most common.[30] Central Taiwan researchers examined the epidemiology of IBD, and 7.9% of all IBD patients had EIMs,[31] with arthritis and psoriasis being the most common in UC patients. A recent examination of IBD clinical presentations using NHIRD data revealed that 11.2% of UC cases between 1998 and 2011 showed gastrointestinal complications and EIMs.[32] During the 14-year study, the prevalence of EIMs increased from 2.8% to 26.6%. This increase was primarily driven by a consistent increase in peripheral arthritis prevalence, which increased from 1% in 1998 to 15.4% in 2011, making it the most common EIM. The increased prevalence of EIMs may be related to physician awareness, increased morbidity, and differing EIM criteria.[32] Notably, significantly higher prevalence of EIMs has been reported in West-

ern countries, ranging from 21% to 40%.[21,33,34] The differences in EIM prevalence between Taiwan and Western countries may be attributed to lower awareness of EIMs in Taiwan and/or potential ethnic differences.[21]

2. Diagnosis

Statement 2.1
The diagnosis of UC is based on medical history, clinical evaluation, and endoscopic and histological findings, especially after the exclusion of infectious etiologies. Level of agreement: Strongly agree, 80.0%; agree, 20.0%; disagree, 0.0%.

Generally, the diagnosis of UC relies on a comprehensive assessment, which includes medical history, clinical evaluation, and the presence of characteristic endoscopic and histological features. Excluding infectious causes should be prioritized since the symptoms of infectious colitis, whether bacterial, viral, or parasitic, can often mimic those seen in UC.[35]

Statement 2.2
A comprehensive medical history of UC and EIMs should be assessed. The most common symptoms include diarrhea, blood/mucus in stool, and/or rectal urgency. Level of agreement: Strongly agree, 80.0%; agree, 20.0%; disagree, 0.0%.

UC has no single diagnostic criteria; hence, its diagnosis primarily relies on recognizing characteristic clinical symptoms. It is crucial to examine patient's medication history, recent travel, food sensitivities, and exposure to infectious diseases to eliminate other potential causes. Furthermore, physicians should evaluate possible manifestations in the eyes, mouth, joints, or skin.[9] The assessment of a patient's disease activity should consider the severity of clinical parameters including stool frequency, stool consistency, bloody mucoid stool, rectal bleeding, and rectal urgency. Accurate classification of disease extent and severity is beneficial in choosing the treatment.[36] The symptoms of chronic diseases are usually insidious, persisting for several weeks or even months, which could be relatively different from diseases of infectious origin which mostly have an abrupt onset. In clinical trials, the clinical UC activity and severity assessment in adults often relies on scoring systems such as the Truelove and Witts criteria and Mayo score.[37,38] Disease severity should be assessed using the Mayo score during follow-up to determine the patient's eligibility for advanced therapy under the NHI.

Statement 2.3
Investigations at diagnosis include markers of disease activity and nutrition status and exclude gastrointestinal infection. Level of agreement: Strongly agree, 76.7%; agree, 23.3%; disagree, 0.0%.

During diagnosis, each patient should undergo a comprehensive biochemical assessment, including a complete blood count, and an assessment of inflammatory markers (e.g., C-reactive protein [CRP]), electrolyte levels, and liver enzymes, and submit stool samples for microbiological and parasite/ova examination, including testing for *Clostridium difficile*.[39,40] Complete blood count may detect thrombocytosis (indicative of an inflammatory response), anemia, and leukocytosis. According to a tertiary center study from Taiwan, among 1,604 IBD patients, 95.3% (471/494) of CD and 87.9% (976/1,110) of UC patients underwent anemia screening. Anemia screening rate in IBD patients significantly increased from 62.6% (162/259) in 2006 to 77.2% (838/1,086) in 2017, and persistent anemia was found in 47.3% (548/1,158) of the screened patients.[41] Elevated inflammatory markers, such as CRP, may be associated with the clinical severity of UC, particularly in acute severe colitis.[40] Fecal calprotectin (FC) is a more sensitive marker than CRP when assessing intestinal inflammation in IBD.[42] Additionally, gastrointestinal infections should be considered in the diagnostic evaluation of IBD.[39,40]

Statement 2.4
Colonoscopy is the mainstay for evaluating UC. The typical endoscopic feature of UC is diffuse, continuous inflammation (loss of vascular pattern, granularity, friability, and ulceration) involving the rectum with or without proximal extension into the colon. Level of agreement: Strongly agree, 80.0%; agree, 20.0%; disagree, 0.0%.

During colonoscopy, at least 2 biopsy samples should be obtained from the inflamed areas.[43] In treatment-naïve UC patients, the typical endoscopic observation is continuous and confluent inflammation affecting the rectum, with or without a continuous extension into the proximal colon. Typically, there is a clear distinction between the inflamed and healthy mucosal areas.[9] Endoscopic signs of mild to moderate disease activity include erythema, mucosal vascular congestion, loss of the visible vascular pattern, granularity, friability, erosions, and shallow ulcerations.[44] Severe UC is characterized by spontaneous bleeding and mucosal ulcerations, and the presence of deep ulcerations has been associated with unfavorable

https://doi.org/10.5217/ir.2023.00050 • Intest Res 2024;22(3):213-249

prognosis.[44,45] Unusual endoscopic features, such as isolated cecal inflammation patches, fragmented inflammation patterns, and rectal sparing, can resemble CD. Therefore, although endoscopic features are crucial, they alone are not specific for a definitive UC diagnosis. Pathological findings and clinical presentations are equally important, particularly in cases with unusual endoscopic features. In addition to its diagnostic utility, colonoscopy enables the evaluation of lesion extent and severity.[9] Nonetheless, full colonoscopy is discouraged in patients with severe colitis to prevent disease exacerbation and increased perforation risk.[46]

Statement 2.5
Endoscopic findings may be atypical, especially in treatment-experienced patients with UC. Level of agreement: Strongly agree, 80.0%; agree, 20.0%; disagree, 0.0%.

Endoscopic features in UC vary by disease severity and treatment history. Typical characteristics are often observed in untreated UC, although some initial-stage cases may exhibit atypical features such as rectal sparing. In treated UC cases, endoscopic and histological findings may show a discontinuous disease pattern characterized by rectal sparing and/or patchy inflammation.[47-49] UC patients who have undergone the treatment of topical mesalamine, glucocorticoids, or systemic therapy may exhibit rectal sparing or a patchy distribution of inflammatory changes.[50,51] The presence of rectal sparing and patchiness should not result in a diagnosis change to CD since these characteristics can also manifest in UC patients.[48,49]

Statement 2.6
Abdominal radiography is recommended for patients with suspected acute severe UC (ASUC) to detect toxic megacolon. Computed tomography (CT) could be indicated to identify complications. Level of agreement: Strongly agree, 60.0%; agree, 40.0%; disagree, 0.0%.

Abdominal radiography is accessible and can detect issues such as colonic dilatation, perforation, and obstruction during acute episodes.[52] Identifying transverse colonic dilatation exceeding 5.5 cm using abdominal radiography remains the radiological criterion for defining toxic megacolon.[53,54] CT scans are beneficial for identifying abdominal complications, such as perforation or ascending pylephlebitis, which may not be detectable clinically or by plain abdominal X-rays.[55] In cases of diagnostic ambiguity or persistent clinical suspicion despite unremarkable radiographic findings, further evaluation should be conducted using CT scans, as they provide superior imaging accuracy.[56]

Statement 2.7
Intestinal ultrasound (IUS) can be used to assess disease extent and severity in patients with UC. Level of agreement: Strongly agree, 26.7%; agree, 63.3%; disagree, 10.0%.

Recent studies have paid significant attention to IUS owing to the demand for noninvasive and readily accessible diagnostic tools to assess disease activity and extent.[57] IUS can make colonoscopy less necessary.

Bowel wall thickness (BWT) is a simple, objective with a high interobserver agreement indicator used for IUS.[58,59] Allocca et al.[60] reported that a BWT of >3 mm, hypoechogenic colonic wall pattern, color Doppler signal (CDS), and lymphadenopathy correlated with endoscopic disease activity. Based on their findings, they developed the Milan ultrasound criteria score ($1.4 \times \text{BWT} + 2.0 \times \text{CDS}$) to assess disease activity in UC, with a threshold of >6.2 detecting patients with active UC with a sensitivity of 85% and specificity of 94%.[60,61] Moreover, Bots et al.[62] developed a UC-IUS index, which includes BWT, CDS, abnormal haustration, and fat wrapping and was strongly correlated with Mayo endoscopic subscores (MES; Spearman's rank correlation coefficient [ρ] = 0.830, $P < 0.001$). However, a limitation of IUS in assessing the rectum should be noted. According to a meta-analysis, the diagnostic accuracy of IUS was lower in the rectum than in the right, transverse, and left colon.[59]

Statement 2.8
The histological diagnosis of UC is based on 2 main components in the lesions: architectural change and inflammatory status. Level of agreement: Strongly agree, 56.7%; agree, 43.3%; disagree, 0.0%.

We recommend utilizing a checklist for histological assessment for comprehensive evaluation and precise diagnosis (Table 1). Mucosal architecture alterations involve glandular distortion (including crypt branching or shortening, crypt widening, and irregular mucosal surface) and epithelial cell irregularities (e.g., Paneth cell metaplasia, goblet cell depletion, and mucin reduction).[16,63] The pathogenesis of crypt architecture and epithelial cell abnormalities is associated with regeneration and repair that occurs after damage.[9]

Histological assessment should further include the presence of dysplasia and malignant alterations. Inflammatory markers include the presence of basal plasmacytosis and degree of neutrophilic or eosinophilic infiltration. Basal plasma-

Table 1. Recommended Checklist for Histological Assessment of UC

Architecture
· Distortion: focal/diffuse
· Mucin/goblet cell depletion: mild/moderate/severe
· Paneth cell metaplasia: present/absent
· Dysplasia: no/low-grade/high-grade
· Adenocarcinoma: present/absent
Inflammatory infiltrates
· Neutrophilic infiltrate: lamina propria/cryptitis/microabscess
· Basal plasmacytosis: present/absent
· Eosinophilic infiltrate: mild/prominent
· Epithelioid granuloma: present/absent
Differential diagnosis
· Tuberculosis infection (acid-fast stain, PCR)
· Amebiasis, CMV infection, pseudomembranous colitis
· Behcet's disease
· Lymphoma
Comments
· No evidence of IBD
· Chronic active colitis, indeterminate
· IBD in favor of: UC/CD
Suggested disease activity scoring using Nancy histological index
· Absence of significant histological disease (grade 0)
· Chronic inflammatory infiltrate with no acute inflammatory infiltrate (grade 1)
· Mildly active disease (grade 2)
· Moderately active disease (grade 3)
· Severely active disease (grade 4)

UC, ulcerative colitis; PCR, polymerase chain reaction; CMV, cytomegalovirus; IBD, inflammatory bowel disease; CD, Crohn's disease.

cytosis refers to the presence of plasma cells between the base of the crypts and muscularis mucosae.[63] Elevated eosinophil levels in the lamina propria has been noted in UC cases. Eosinophils are a common inflammation marker; hence, they may be found in other types of colitis. When eosinophil levels are extremely high, eosinophilic colitis should be considered as a potential differential diagnosis.[64] In contrast, well-formed epithelioid granulomas within the lamina propria indicate CD rather than UC.[65]

The Nancy histological index comprises 3 descriptors and 5 classification levels. It has been validated for practical application in clinical practice and clinical trials, particularly in UC cases.[66] The committee proposes using the Nancy index in UC diagnosis to evaluate histological disease activity. Moreover, reviewing and assessing prior biopsy slides is recommended when diagnosing UC. Segmental biopsy specimens are crucial in diagnosing and classifying IBD and differentiating it from other intestinal inflammatory conditions.[67]

Statement 2.9
The major role of pathology in diagnosing UC is to exclude other etiologies, such as infection, malignancy, etc. Level of agreement: Strongly agree, 63.3%; agree, 36.7%; disagree, 0.0%.

Distinguishing UC from CD at the microscopic level can be challenging. Additionally, pathological examinations can rule out infectious colitis, such as pseudomembranous colitis, tuberculosis (TB), amebiasis, and cytomegalovirus (CMV) colitis, and malignancies, such as lymphoma or colorectal cancer (CRC).[68] Besides infections and malignancies, several conditions can mimic UC during histological examination, such as Behcet's disease, endometriosis, thermal injury, ischemic bowel, and diverticulitis.

3. Specific Considerations

Statement 3.1
Hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and hepatitis B core antibodies (anti-HBc) should be routinely checked before treatment initiation, especially before the initiation of immunomodulators, steroids, and advanced therapy. Level of agreement: Strongly agree, 73.3%; agree, 26.7%; disagree, 0.0%.

Hepatitis B virus (HBV) is endemic globally; however, its prevalence significantly varies across geographic regions.[69] Asia and Africa collectively account for 68% of all individuals infected with HBV, with a prevalence of ≥8%. HBV infection prevalence is lower in Western countries, typically <2%.[70] A study conducted in a hospital in Taiwan revealed that the seroprevalence of HBsAg was 15.4% among 110 UC patients.[31] Another multicenter study conducted in Taiwan enrolled 274 IBD patients and demonstrated that the HBsAg seropositive rate was 10.2% for UC and 5.5% for CD patients.[71]

Furthermore, a recent systematic review of 34 studies indicated that the pooled prevalence of HBsAg and anti-HBc was 3.3% and 14.2%, respectively.[72] HBV infection prevalence among UC patients is comparable to that of the general population with regional variations.[72] Reactivation of viral hepatitis can lead to life-threatening outcomes, and it has been widely reported in patients undergoing immunosuppressive therapy.[73]

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Before starting immunomodulating or immunosuppressive therapy for UC, HBV screening is critical to reduce the risk of HBV reactivation.[31,74] A recommended approach is administering HBV vaccination to individuals who test negative for HBsAg, anti-HBs, and anti-HBc. Routine serologic testing should be conducted to assess the immune response to HBV vaccination within 1–3 months after vaccination.[75] A recent study revealed that among 158 IBD patients with available data, HBsAg seroprevalence was 13.3% (CD 11.3%, UC 15.4%).[31] Among IBD patients who tested positive for HBsAg, 15.3% tested positive for the hepatitis B e antigen, and 61.0% had detectable HBV DNA. These findings highlight the importance of testing and prophylactic use of antiviral treatment to decrease the risk of HBV reactivation.

Statement 3.2
In patients who are HBsAg and/or anti-HBc positive, HBV DNA quantification is recommended before the initiation of steroids, immunomodulators, biologics, and small molecules. Level of agreement: Strongly agree, 56.7%; agree, 43.3%; disagree, 0.0%.

Occult HBV infection may be present in patients who are positive for anti-HBc and negative for HBsAg. However, occult HBV reactivation is rare during IBD immunosuppressive therapy.[74] Liver dysfunction was observed in 25%–36% of IBD patients who tested positive for HBsAg.[76,77] HBV reactivation occurs in IBD patients with prior HBV infections who have undergone extended immunomodulatory therapy, are positive for HBV DNA, or have not received prophylactic antiviral treatment.[74] In HBsAg-negative, anti-HBc-positive individuals, reactivation is the reappearance of HBsAg or detection of HBV DNA.[78] Therefore, monitoring HBV DNA levels in these patients is critical.

Statement 3.3
In patients positive for HBsAg and/or with detectable HBV DNA, preventing HBV reactivation should be considered. Level of agreement: Strongly agree, 70.0%; agree, 30.0%; disagree, 0.0%.

In IBD patients who carry HBV and test positive for HBsAg or have detectable HBV DNA, prophylactic antiviral therapy using nucleotide/nucleoside analogs should be initiated. This treatment should be started 1–2 weeks before immunomodulatory therapy and sustained for 6–12 months after discontinuing immunomodulatory treatment.[56,58] Liver transaminase levels and HBV DNA titers should be monitored regularly throughout the antiviral treatment course.[73] Entecavir and tenofovir are preferred for IBD patients because of their high antiviral effectiveness and low long-term resistance rates.[74] In Taiwan, the NHI reimburses anti-HBV treatment for patients prescribed prednisolone at a daily dosage of ≥20 mg for over 1 month.[79]

Statement 3.4
Screening for TB infection with chest radiography and interferon-gamma release (IGRA) assays or tuberculin skin test (TST) is recommended before initiating advanced therapy in patients with UC. Level of agreement: Strongly agree, 80.0%; agree, 20.0%; disagree, 0.0%.

Patients with IBD are at a higher risk for active TB infections than the general population because of their use of immunomodulating treatments.[74] A systematic review reported that the most common infections after treatment with biologics and small-molecule drugs were candidiasis (in the oropharynx and other locations), followed by TB.[80] Furthermore, in patients treated with anti-tumor necrosis factor (TNF), TB presentation tends to be more atypical, involve extrapulmonary sites, and become disseminated, which can complicate the diagnosis.[74] In Taiwan, approximately 5.8% of extrapulmonary TB cases have been reported to involve the gastrointestinal tract.[81] A multicenter study in Taiwan included 274 IBD patients and showed that the IGRA positive rate was 3.3 for UC and 3.1 for CD patients.[71] Furthermore, a retrospective study conducted in Taiwan examined the prevalence of latent TB (LTB) in IBD patients before and after biological treatments and revealed that the prevalences were comparable to those in other Asian countries but higher than those in most Western countries.[82]

In Taiwan, before starting advanced therapies, UC patients should undergo screening for LTB, including a physical examination, chest X-ray, and either a TST or an IGRA.[16,75] Notably, prior Bacille Calmette-Guérin (BCG) vaccination can influence TST but not IGRA results.[83] The Taiwan Centers for Disease Control (CDC) recommends using the TST only for individuals <5 years or unable to complete the IGRA. Since 2016, the IGRA has been used for individuals aged ≥5 years to minimize false positives caused by cross-reactivity with the BCG vaccine and avoid unnecessary LTB infection treatments.[84]

Statement 3.5
In patients diagnosed with LTB, prophylactic treatment to prevent TB reactivation should be started at least 4 weeks

prevent TB reactivation should be started at least 4 weeks before using advanced therapy. Level of agreement: Strongly agree, 73.3%; agree, 26.7%; disagree, 0.0%.

Patients with suspected LTB or active TB should receive anti-TB treatment before starting advanced therapies (biologics or small molecules).[75] Chemoprophylaxis significantly reduces the risk of TB reactivation in patients with LTB. LTB treatment should follow the current Taiwan CDC guideline.[84] At least 4 weeks of TB treatment should be administered before starting biologic therapy. TB chemoprophylaxis typically involves isoniazid for 6–9 months. Consultation with an infectious disease or chest specialist for multidisciplinary care is highly recommended.[16,74] There is no specific guidance for managing LTB infections in patients requiring small-molecule therapies; however, it is advisable to provide 4 and 3 weeks of LTB treatment before starting Janus kinase (JAK) and calcineurin inhibitors, respectively. These recommendations are based on clinical trials conducted for other medical conditions.[85]

Statement 3.6
During advanced therapy, patients should be monitored for signs and symptoms of active TB with chest X-ray and IGRA or TST performed at least annually. Level of agreement: Strongly agree, 73.3%; agree, 26.7%; disagree, 0.0%.

Patients with IBD undergoing advanced therapy should be monitored for signs and symptoms of active TB. Chest radiography and IGRA assessments should be conducted every 6 months or at least annually for the IGRA.[16] Anti-TB therapy should be initiated when active TB is diagnosed. Further, anti-TNF therapy should be discontinued but can be resumed after a 2-month anti-TB therapy.[74]

Statement 3.7
Vaccination before starting immunosuppressive treatment. Level of agreement: Strongly agree, 33.3%; agree, 66.7%; disagree, 0.0%.

Statement 3.7.1
HBV vaccination is recommended in patients who are negative for HBsAg, anti-HBs, and anti-HBc.

Patients with IBD who test negative for all these 3 serological markers are susceptible to HBV infection and vaccination is currently advised.[74] Nonetheless, IBD patients have shown a reduced response to HBV vaccination.[86] Therefore, IBD patients should receive HBV vaccination and have their anti-HBs antibody level assessed 1–3 months after vaccination.[71]

Statement 3.7.2
Herpes zoster (HZ) vaccine is recommended for patients before immunosuppressive therapy, or at least for immunocompetent patients aged more than 50 years.

Patients with IBD exhibit a higher risk of HZ infection compared to those without IBD, with an incidence rate ratio of 1.49 (95% confidence interval [CI], 1.34–1.65) for UC.[87] Furthermore, this risk varies with the dose and class of treatment. JAK inhibitors were the drug class most likely to increase the risk of infection, and the risk increased with higher doses. Tofacitinib at 10 mg twice a day (relative risk [RR], 6.90; 95% CI, 1.56–30.63) and upadacitinib at 45 mg daily (RR, 7.89; 95% CI, 1.04–59.59) were more likely to increase risk of HZ infection.[88]

The recombinant HZ vaccine (RZV) is recommended for IBD patients because of its effectiveness and safety.[89] Patients with IBD have an elevated risk of HZ infections, which remains higher regardless of disease duration.[90] In 2018, the US CDC recommended RZV vaccination for individuals undergoing low-dose immunosuppressive therapy (e.g., <20 mg/day of prednisone or equivalent), planned for immunosuppression, or recovering from an immunocompromizing illness.[91] Therefore, administering HZ vaccine to IBD patients on immunosuppression is appropriate.[90] Both the American College of Gastroenterology (ACG) and ECCO guidelines recommend HZ vaccination for IBD patients aged ≥50 years.[89,90] Since the live HZ vaccine is unsuitable for patients on immunosuppressive therapy, RZV is preferred. RZV can further be considered for patients aged 19–49 years with specific risk factors.[92]

Statement 3.7.3
Human papillomavirus (HPV) vaccination is recommended for patients younger than 26 years old.

Numerous studies have demonstrated that immunosuppressive treatments potentially increase the risk of persistent HPV infection and, consequently, cervical cancer. Despite limited data on the relationship between IBD and HPV, a cross-sectional study underscored a markedly elevated HPV 16/18 cervical infection rate in IBD patients compared to controls (7.3% vs. 0.3%: odds ratio [OR], 29.04; 95% CI, 3.64–210.99; $P<0.001$). Further investigation indicated that methotrexate exposure (OR, 4.76; 95% CI, 1.47–15.40; $P<0.005$) and using more than 2 types of immunosuppressants (OR, 3.64; 95% CI, 1.26–10.56; $P<0.013$) significantly increased the risk of HPV infection.[89]

The nonavalent vaccine is currently preferred in national

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recommendations.[89] Most local guidelines advocate for routine HPV vaccination of males and females aged 11–14 years with a 2-dose regimen and offer catch-up vaccination beyond this age. The vaccine is suitable for administration starting at age 9 years. A 3-dose regimen is recommended if HPV vaccination commences at age ≥15 years.[89] While HPV vaccination is advised for females aged 9–26 years, most females in this age range may have already been exposed to HPV; hence, regular screening is the most effective approach for safeguarding females against cervical cancer. The American College of Obstetricians and Gynecologists and the U.S. CDC recommend annual screening for females with a history of chronic immunosuppression.[90]

The link between IBD and cervical dysplasia/cancer remains unclear; however, the risk appears to be elevated in patients receiving immunosuppressive therapy, such as corticosteroids, immunomodulators, and anti-TNF agents. Several guidelines advocate for HPV vaccination for individuals aged 18–26 years, including those with IBD.[89,93] While the recently issued Canadian guidelines do not specifically recommend HPV vaccination for individuals aged 27–45 years, it should be considered based on the patient's risk factors (e.g., the potential for new sexual partners or future immunosuppressive therapy) and their personal preferences.[92] A small study found that HPV vaccination resulted in favorable immunogenicity and no serious adverse events in female IBD patients undergoing immunosuppressive therapy.[92]

4. Evaluation and Treatment Goals

Statement 4.1
Clinical classification (Montreal classification) and activity scores (Mayo score for adults and Pediatric UC Activity Index [PUCAI] for children) are recommended for the assessment of patients with UC. Level of agreement: Strongly agree, 90.0%; agree, 10.0%; disagree, 0.0%.

Table 2. Montreal Classification for Extent of UC

Extent	Anatomy
E1: Ulcerative proctitis	Involvement limited to the rectum (i.e., proximal extent of inflammation is distal to the rectosigmoid junction)
E2: Left-sided UC (distal UC)	Involvement limited to a proportion of the colorectum distal to the splenic flexure
E3: Extensive UC (pancolitis)	Involvement extends proximal to the splenic flexure

UC, ulcerative colitis.

There was no formal clinical classification of UC similar to the Vienna classification of CD; thus, a working group of investigators reviewed the current clinical evidence of UC classification in 2003, revealing the Montreal classification at the 2005 Montreal World Congress of Gastroenterology (Tables 2 and 3).[94,95]

The Mayo score is a widely accepted and recommended instrument for disease severity evaluation. Initially introduced by Schroeder et al.[38] in 1987 during a clinical trial assessing 5-aminosalicylic acid (5-ASA) drugs for UC, the Mayo score serves as a combined endoscopic and clinical tool for evaluating UC severity. This comprehensive score incorporates subscores from 4 categories (stool frequency, rectal bleeding, flexible proctosigmoidoscopy or colonoscopy findings, and physician's global assessment), yielding a total score from 0 to 12. In the endoscopic component, a score of 0 signifies normal mucosa or inactive UC; 1, mild disease characterized by mild friability, reduced vascular pattern, and mucosal erythema; 2, moderate disease with friability, erosions, complete loss of vascular pattern, and significant erythema; and 3, ulceration and spontaneous bleeding.[44]

For the pediatric group, the use of PUCAI (Table 4) proved highly feasible in an outpatient clinical practice setting, with over 96% of visits encompassing all 6 essential components for its calculation.[96] The researchers successfully established a strong correlation between PUCAI and physician global assessment using various analytical approaches, a PUCAI score at least 65 is defined ASUC in children.[96]

Statement 4.2
Macro- and micronutrient deficiencies are prevalent in patients with UC. Adequate nutritional assessment, monitoring, and support are recommended. Level of agreement: Strongly agree, 53.3%; agree, 46.7%; disagree, 0.0%.

Table 3. Montreal Classification for Severity of UC

Severity	Definition
S0: Clinical remission	Asymptomatic
S1: Mild UC	Passage of 4 or fewer stools/day (with or without blood), absence of any systemic illness, and normal inflammatory markers (ESR)
S2: Moderate UC	Passage of more than 4 stools per day but with minimal signs of systemic toxicity
S3: Severe UC	Passage of at least 6 bloody stools daily, pulse rate of at least 90 beats/min, temperature of at least 37.5°C, hemoglobin of less than 10.5 g/100 mL, and ESR of at least 30 mm/hr

UC, ulcerative colitis; ESR, erythrocyte sedimentation rate.

Table 4. The Pediatric Ulcerative Colitis Activity Index Components

Item	Point
1. Abdominal pain	
No pain	0
Pain can be ignored	5
Pain cannot be ignored	10
2. Rectal bleeding	
None	0
Small amount only, in < 50% of stools	10
Small amount with most stools	20
Large amount (> 50% of stool content)	30
3. Stool consistency of most stools	
Formed	0
Partially formed	5
Completely unformed	10
4. Number of stools per 24 hr	
0–2	0
3–5	5
6–8	10
> 8	15
5. Nocturnal stools (any episode causing wakening)	
No	0
Yes	10
6. Activity level	
No limitation of activity	0
Occasional limitation of activity	5
Severe restricted activity	10
Sum of Pediatric Ulcerative Colitis Activity Index	0–85

The documented prevalence of malnutrition among IBD patients varies from 20% to 85%.[97] Micronutrient deficiencies commonly observed in IBD patients include iron, calcium, selenium, zinc, magnesium, water-soluble vitamins such as B_{12} and folic acid, and fat-soluble vitamins (A, D, E, and K). Osteopenia and osteoporosis are common in both male and female IBD patients, affecting approximately 20%–50%.[97]

Several factors contribute to these issues, including the cumulative use of corticosteroids, extensive small bowel disease or resection, chronic inflammation, physical inactivity, and deficiencies in calcium, vitamins, and other micronutrients.[97] Specifically, calcium deficiency is prevalent in roughly 13% of patients with CD and 10% of patients with UC, and up to 70% of patients with CD and 40% of patients with UC have low vitamin D levels.[97] All patients should be evaluated for malabsorption parameters, including weight and anemia. Screening for anemia every 3 months is recommended for those with symptoms indicative of an active disease.[43] Furthermore, measuring vitamin D levels is encouraged in symptomatic patients.[43] Parenteral nutrition (PN) is recommended only when enteral nutrition (EN) has been proven ineffective or infeasible. Elemental diets are generally discouraged, and evidence to favor any specific formula when designing nutritional regimens are limited.[98] If malnutrition is detected, surgery for UC should be postponed by 7–14 days, during which intensive medical nutrition can be provided.[99] In emergency cases where surgery is urgently needed, medical nutrition (EN or PN) should be initiated if the patient is malnourished at the time of surgery or if oral diet cannot be resumed within 7 days after surgery.

Statement 4.3
The treatment of UC depends on the severity and extent of disease. The goals of treatment include induction and maintenance of remission, prevention of complications, and improving QoL. Level of agreement: Strongly agree, 83.3%; agree, 16.7%; disagree, 0.0%.

Therapeutic decisions for UC should be based on factors such as the endoscopic extent of inflammation; disease severity; prognostic indicators for poorer outcomes, including age < 40 years at diagnosis, extensive disease, or the presence of EIMs; and the patient's response to prior treatments.[100-102] The treatment aims to achieve complete remission, that is, long-lasting relief from symptoms and endoscopic remission without corticosteroid therapy, while providing appropriate psychosocial support, maintaining a normal health-related QoL, preventing complications such as hospitalization and surgery, and averting cancer risk.[100,103] Additionally, treatment should be customized based on the distribution and pattern of the disease, prior treatment response, comorbidities, and the delicate balance between treatment effectiveness and potential side effects.[16]

Based on the updated "Selecting Therapeutic Targets in Inflammatory Bowel Disease-II (STRIDE-II)" recommendation, the primary long-term treatment objectives for individuals include clinical remission, endoscopic healing (EH), improved QoL, and preventing disability. Immediate treatment focuses on providing symptomatic relief and the use of serum and fecal biomarkers as intermediate, medium-term treatment targets.[104]

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5. Treatment

Statement 5.1
Nutrition. Level of agreement: Strongly agree, 53.3%; agree, 46.7%; disagree, 0.0%.

Statement 5.1.1
EN appears safe, and PN is recommended for patients with UC when they cannot tolerate EN or its associated complications such as toxic megacolon, etc.

Dietary restrictions are typically unnecessary for most patients with UC. However, EN or PN may be considered with severe exacerbations and during the perioperative phase.[105] Among these, EN is preferred owing to its considerably lower risk of complications, particularly in patients with acute UC. While EN's suitability for active UC has not been thoroughly assessed, it appears to be a safe and nutritionally adequate option for patients with severe disease.[106] Further studies with larger patient cohort are required to validate its efficacy.[10,99] While there are no explicit contraindications for using PN in UC, bowel rest through intravenous (IV) nutrition does not significantly affect the overall outcome.[99] PN is recommended for malnourished patients with UC, particularly those with severe disease, when they cannot tolerate EN or when bowel rest is indicated.[10,107,108]

Statement 5.1.2
All patients with UC should undergo counseling by a dietician as part of the multidisciplinary approach to improve nutritional therapy and avoid malnutrition and nutrition-related complications.

In many European countries, nutritional screening is vital to gastrointestinal care.[99] Nutritional screening at diagnosis and during regular check-ups is highly proposed for IBD patients. Patients with IBD have a risk of malnutrition; hence, nutritional care is crucial in their treatment. This includes managing nutrient deficiencies, preventing osteoporosis, and promoting optimal growth and development in children. Nutritional screening can help medical staff identify patients at risk for malnutrition and ensure they receive appropriate treatment to avoid complications, ultimately enhancing their overall QoL.[99] Hsieh et al.[109] reported that when patients with UC achieved clinical remission, dietary restrictions may negatively affect their social lives, underscoring the need for tailored dietary guidance to mitigate these impacts and improve QoL.

Statement 5.2
Conventional therapy. Level of agreement: Strongly agree, 46.7%; agree, 53.3%; disagree, 0.0%.

Statement 5.2.1
Induction of remission in patients with mild to moderate UC.

Statement 5.2.1.1
For patients with mildly active ulcerative proctitis, topical 5-ASA therapies at a dose of 1 g/day is recommended to induce remission.

Statement 5.2.1.2
For patients with mildly to moderately active left-sided UC, a combination of topical 5-ASA at a dose of at least 1 g/day and oral 5-ASA at a dose of at least 2 g/day is recommended.

Statement 5.2.1.3
For patients with mildly to moderately active extensive colitis, oral 5-ASA at a dose of at least 2 g/day with supp/enema is recommended to induce remission.

The preferred initial treatment for patients with mild to moderate UC of any extent is 5-ASA therapy. According to the ACG guidelines, oral 5-ASA at a minimum dose of 2 g/day is recommended for patients with mildly active extensive UC.[100-102] For patients with mildly active left-sided UC, combining rectal 5-ASA enema at a minimum dose of 1 g/day with oral 5-ASA at a minimum dose of 2 g/day is more effective in relieving symptoms than oral 5-ASA alone.[110,111] Additionally, 5-ASA monotherapy has been approved to be effective and safe for moderately active UC. A meta-analysis revealed that 5-ASA at 2.4 g/day was beneficial for patients with moderately active UC, whereas corticosteroid therapy was more effective for patients with severe UC.[112]

Statement 5.2.2
For patients with mildly to moderately active UC not responding to 5-ASA, we recommend adding budesonide multi-matrix (MMX) at a dose of 9 mg/day to induce remission.

Budesonide MMX is a corticosteroid that reduces inflammation in the colon through a colonic release mechanism, minimizing systemic bioavailability and side effects.[101] It is suitable for patients with mild to moderate UC who are intolerant or unresponsive to 5-ASA, specifically those with left-sided or extensive UC. Switching to another 5-ASA formulation is not advised. For patients with mild to moderate UC, nonsystemic corticosteroids such as budesonide MMX should be consid-

ered before resorting to systemic therapy. However, this medication has not been studied for inducing remission in patients with moderate to severe UC.[100]

Statement 5.2.3
Induction of remission in patients with moderate to severe UC.

Statement 5.2.3.1
For patients with mild to moderate UC who fail 5-ASA and/or budesonide MMX induction and those with moderate to severe UC, we recommend systemic corticosteroids to induce remission.

Statement 5.2.3.2
For patients with severe UC, IV corticosteroids is recommended.

Oral corticosteroids for symptom relief should be considered for patients with moderate to severe UC who do not show improvement with oral 5-ASA therapy, those who are currently taking ≥2 g/day of 5-ASA or immunomodulators for maintenance therapy but suffer a relapse, those with persistent rectal bleeding for more than 2 weeks, and those who still have abdominal symptoms after 6 weeks of sufficient 5-ASA therapy.[101] Notably, proper UC therapy requires minimizing the duration of systemic corticosteroid treatment and initiating steroid-sparing therapy promptly. The rate of tapering should be determined based on clinical symptoms, total steroid exposure, and the time it takes for alternative therapies to start working. Corticosteroids such as oral prednisone are typically given as a single dose, with an initial dose of 40–60 mg/day.[100] For moderate active disease, an appropriate treatment regimen is to start with a prednisone dose of 40 mg/day for 1 week, followed by a weekly reduction of 5 mg/day, establishing an 8-week course. Initial prednisolone doses of ≤15 mg/day were found to be ineffective for treating active disease.[100,101]

For patients who do not respond adequately to conventional oral corticosteroids, stool should be retested for bacteria, parasites, and *C. difficile* toxin. Sigmoidoscopy with biopsies should be performed to rule out CMV colitis. IV corticosteroid therapy may be initiated after infectious diseases have been ruled out.[103] A noticeable clinical improvement is typically expected within 7–10 days of IV corticosteroid therapy.[113] After excluding infection complications such as coexistent CMV or *C. difficile*-associated disease, patients are diagnosed with active steroid-refractory UC if their condition does not improve within 4 weeks of corticosteroid therapy using an oral prednisolone equivalent dose of 0.75–1 mg/kg body weight or at least 1 week of IV corticosteroids. For patients with active steroid-refractory UC, the primary treatment option is advanced therapy.[103]

Statement 5.2.4
Maintenance of remission in patients with mild to moderate UC.

Statement 5.2.4.1
For patients who previously responded to 5-ASA induction treatment, retaining 5-ASA treatment as the maintenance therapy is recommended.

For patients who previously responded to 5-ASA induction therapy, 5-ASA should be continued as maintenance therapy. Further, 5-ASA at a rectal dosage of 1 g/day and an oral dosage of ≥2 g/day is recommended for patients with mildly active ulcerative proctitis and those with mildly active left-sided or extensive UC, respectively, to maintain remission.[100] Patients with extensive UC or frequent relapses may benefit from a higher 5-ASA dose as maintenance therapy. A systematic review examining the efficacy and safety of 5-ASA compared to placebo showed a statistically significant benefit with 5-ASA dosages of 1.0–1.9 g/day (RR, 0.65; 95% CI, 0.56–0.76) and ≥2 g/day (RR, 0.73; 95% CI, 0.60–0.89). Furthermore, high-dose 5-ASA appears to be equally safe as low-dose 5-ASA and is not associated with a higher incidence of adverse events.[114]

Statement 5.2.4.2
Steroid free is the goal of long-term treatment. Therefore, we recommend against corticosteroids for maintenance of remission in patients with UC.

Corticosteroid therapy is associated with several potential adverse side effects, including diabetes, hypertension, infection, and osteoporosis.[115] Patients treated with long-term corticosteroids are at increased risk of serious or opportunistic infections.[115] Mood disorders develop in up to 60% of patients receiving corticosteroid treatment, with severe psychiatric reactions, including psychotic and affective symptoms, developing in approximately 5%.[115] Although corticosteroids can induce remission in UC, they are not recommended for long-term maintenance therapy.

Statement 5.2.4.3
For patients with steroid dependence, we suggest bridging to thiopurine or advanced therapies for maintenance of remission.

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The UK and European guidelines recommend a starting dose of 40 mg/day of oral prednisolone and reduction by 5 mg/day at weekly intervals, resulting in an 8-week course.[116] Shorter treatment courses in active UC lead to early relapse, with starting prednisolone doses of 15 mg/day or less being ineffective. Furthermore, prolonged corticosteroid use increases the risk of steroid dependence, where symptoms relapse upon reducing the dose <20 mg or after discontinuation, usually within months.[116,117] An alternative therapeutic strategy, such as thiopurine or advanced therapies, may be considered for long-term UC management. Thiopurines, such as azathioprine (AZA) and 6-mercaptopurine (6-MP), are immunomodulators that effectively maintain remission in patients who do not respond to or depend on corticosteroids. Moreover, they can be considered for patients who fail or cannot tolerate mesalamine or sulfasalazine.[118]

Statement 5.2.4.4
Patients with steroid- or immunomodulator-refractory disease should be treated with advanced therapies or tacrolimus.

After excluding CMV colitis, *C. difficile*-associated disease, or cancer, IV steroid treatment could be considered for patients with active steroid-refractory UC. However, in a retrospective study of 110 episodes of disease refractory to oral steroids, nearly half of the patients developed early IV steroid therapy dependency.[101]

All approved advanced therapy could be considered for steroid-refractory or immunomodulator-refractory UC. Considering its availability, tacrolimus is an alternative treatment for corticosteroid-refractory patients and has demonstrated short-term effectiveness. Regularly monitoring for adverse effects, such as nephrotoxicity and opportunistic infections, is critical. AZA/6-MP is indicated in patients who respond positively to tacrolimus for long-term maintenance therapy.

Statement 5.3
Advanced therapy. Level of agreement: Strongly agree, 46.7; agree, 53.3%; disagree, 0.0%.

Statement 5.3.1.1
Anti-TNF agents (infliximab, adalimumab, and golimumab) are recommended for induction and maintenance of remission in patients with moderately to severely active UC.

Statement 5.3.1.2
When infliximab is used for patients with moderately to severely active UC, combination with thiopurine is suggested.

Infliximab, adalimumab, and golimumab have shown effectiveness in inducing remission in patients with moderately to severely active UC. When introducing anti-TNF therapy, especially infliximab, combining it with thiopurine is recommended.[100] Regular monitoring of white blood cell counts and 6-thioguanine levels (a thiopurine metabolite) is crucial in patients under thiopurine therapy. The benefits and risks of thiopurine therapy should be carefully balanced for long-term treatment.[119] In the ACT 1 and 2 trials, UC patients treated with infliximab were more likely to show a clinical response than those receiving placebo at weeks 8 and 30 ($P<0.001$).[120] The ULTRA2 trial demonstrated the efficacy of adalimumab. In anti-TNF-naïve patients, remission rates were higher with adalimumab than with the placebo at weeks 8 ($P=0.017$) and 52 ($P=0.029$). In patients with prior exposure to anti-TNF agents, remission rates with adalimumab were comparable to the placebo at week 8 ($P=0.559$) but higher than the placebo at week 52 ($P=0.039$).[121] The PURSUIT-Maintenance trial demonstrated the efficacy of golimumab in UC patients. More patients treated with 100 mg of golimumab achieved clinical remission and mucosal healing than those who received the placebo ($P=0.004$ and $P=0.002$, respectively).[122] Notably, the results were consistent in the Japanese population.[123]

Statement 5.3.2
Vedolizumab is recommended for induction and maintenance of remission in patients with moderately to severely active UC.

Vedolizumab is a humanized monoclonal antibody that specifically targets the integrin α4β7 heterodimer, inhibiting lymphocyte movement in the gut without affecting their transport to the central nervous system. The GEMINI 1 trial demonstrated that vedolizumab had superior efficacy to the placebo in induction and maintenance therapy for UC.[124] At week 52, 41.8% of patients on vedolizumab every 8 weeks and 44.8% on vedolizumab every 4 weeks achieved clinical remission, whereas only 15.9% of patients who switched to the placebo achieved clinical remission (both $P<0.001$).[124] The VISIBLE 1 trial demonstrated that, after open-label IV vedolizumab (300 mg) at weeks 0 and 2, subcutaneous vedolizumab (108 mg) every 2 weeks had comparable efficacy to IV vedolizumab (300 mg) every 6 weeks.[125] Therefore, IV and subcutaneous vedolizumab administrations are effective in maintaining remission in patients with moderate to severe UC. The VIOLET study in Taiwan revealed that vedolizumab therapy led to clinical response, clinical remission, steroid-free remission, and muco-

sal healing in 76.0%, 58.0%, 35.0%, and 62.2% of UC patients, respectively, within 1 year.[71]

The VARSITY trial involved 769 patients with moderately to severely active UC who were administered vedolizumab or adalimumab. By week 52, more patients achieved clinical remission and showed improved endoscopic outcomes in the vedolizumab group than in the adalimumab group (31.3% vs. 22.5%, $P=0.006$ and 39.7% vs. 27.7%, $P<0.001$; respectively).[126] The American Gastroenterological Association (AGA) guidelines recommend infliximab or vedolizumab instead of adalimumab for inducing remission in adult outpatients with moderately to severely active UC who are naïve to biologic agents.[127] Based on a network meta-analysis, vedolizumab is an effective first-line therapy for patients with moderately to severely active UC, and is associated with a lower risk of infections than golimumab and tofacitinib.[128]

Statement 5.3.3
Antibodies targeting interleukin (IL)-12/23 (ustekinumab) or IL-23 (mirikizumab) are recommended for induction and maintenance of remission in patients with moderately to severely active UC.

Ustekinumab targets the p40 subunit common to IL-12 and IL-23, crucial cytokines that regulate the function of T-helper 1 and 17 cell subsets. This mechanism prevents the interaction between IL-12 and IL-23 receptor complexes.[129] At week 44 of the UNIFI trial, the clinical remission rate was significantly higher among patients given subcutaneous ustekinumab every 12 (38.4%) or 8 (43.8%) weeks than among those given the placebo (24.0%; $P=0.002$ and $P<0.001$, respectively).[130] Additionally, a meta-analysis indicated a potential benefit of ustekinumab over adalimumab and vedolizumab for patients with prior exposure to anti-TNF agents (ustekinumab vs. vedolizumab: OR, 5.99; 95% CI, 1.13–31.76; ustekinumab vs. adalimumab: OR, 10.71; 95% CI, 2.01–57.20).[128]

The LUCENT-1 and LUCENT-2 trials evaluated the efficacy and safety of mirikizumab, the anti-IL-23p19 antibody, in patients with moderately to severely active UC who had failed conventional and biologic therapies previously and/or JAK inhibitors and required additional treatment. In the LUCENT-2 trial, 49.9% (182/365) of patients treated with mirikizumab achieved clinical remission within 1 year, compared to 25.1% (45/175) of those treated with the placebo. Notably, almost all patients who achieved clinical remission with mirikizumab at 1 year had not taken corticosteroids for at least 3 months before the end of maintenance treatment (97.8%, 178/182).[131]

Statement 5.3.4
JAK inhibitors (tofacitinib, upadacitinib, and filgotinib) are recommended for induction and maintenance of remission in patients with moderately to severely active UC.

Tofacitinib, which inhibits JAK1, JAK3, and JAK2, was the first JAK inhibitor approved for UC.[132] The OCTAVE trials demonstrated that tofacitinib effectively induced remission in patients with moderately to severely active UC. The remission rates with tofacitinib and placebo at week 8 were 18.5% and 8.2% in the OCTAVE Induction 1 trial and 16.6% versus 3.6% in the OCTAVE Induction 2 trial, respectively.[133] In the OCTAVE Sustain trial, remission rates in week 52 were 34.3%, 5 mg tofacitinib group; 40.6%, 10 mg tofacitinib group; and 11.1%, placebo group.[133] Tofacitinib appeared effective in anti-TNF-naïve and anti-TNF-experienced patients. While the infection risk seemed to increase in patients treated with tofacitinib (OR, 1.51; 95% CI, 1.05–2.19), the incidence of serious infections did not differ significantly between tofacitinib and placebo.[134] Furthermore, Singh et al.[128] determined a possible benefit of tofacitinib over adalimumab or vedolizumab for patients with prior anti-TNF exposure (tofacitinib vs. adalimumab: OR, 11.05; 95% CI, 1.79–68.41; tofacitinib vs. vedolizumab: OR, 6.18; 95% CI, 1.00–38.00).

Upadacitinib, a selective small molecule that inhibits JAK1, demonstrated efficacy and safety in treating UC in the U-ACHIEVE and U-ACCOMPLISH trials.[135] Clinical remission rates at week 8 with upadacitinib and the placebo were 26% and 5% in the U-ACHIEVE trial and 34% and 4% in the U-ACCOMPLISH trial, respectively. Upadacitinib was more effective than the placebo in achieving clinical remission, had lower rates of adverse events, and did not increase the risk of infection.[135-137]

Filgotinib, another selective JAK1 inhibitor, was approved for the treatment of patients with moderate to severe UC. The SELECTION trial evaluated the efficacy of filgotinib for induction and maintenance therapy for UC patients.[133] At week 10, more patients given filgotinib (200 mg) were in clinical remission than those given the placebo in the biologic-naïve (26.1% vs. 15.3%, $P=0.016$) and biologic-experienced (11.5% vs. 4.2%, $P=0.01$) groups. At week 58, 37.2% of patients given filgotinib (200 mg) were in clinical remission compared to 11.2% of those given placebo ($P<0.0001$).[138]

Statement 5.3.5
Ozanimod is recommended for induction and maintenance of remission in patients with moderately to severely active UC.

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Ozanimod is a sphingosine-1-phosphate (S1P) receptor modulator, exhibiting strong binding affinity to S1P subtypes 1 and 5. This interaction results in the internalization of S1P subtype 1 receptors in lymphocytes, preventing their mobilization from the lymph nodes to inflammatory sites. In the True North phase 3 trial, ozanimod proved effective and safe for moderately to severely active UC, achieving significantly higher clinical remission rates than placebo during induction (18.4% vs. 6.0%, $P<0.001$) and maintenance phases (37.0% vs. 18.5%, $P<0.001$).[139]

Statement 5.4
Management of ASUC. Level of agreement: Strongly agree, 36.7%; agree, 63.3%; disagree, 0.0%.

Statement 5.4.1
Approximately 20%–25% of patients with UC experience at least one severe acute exacerbation, often necessitating hospitalization, throughout their disease journey.

About 20% of patients with UC experience severe flares, leading to ASUC, and require hospitalization.[136] In ASUC patients, particularly those under immunosuppression, concurrent infections (especially *C. difficile* and CMV) should be ruled out. The first-line therapy for ASUC is IV corticosteroids. If patients do not respond to IV corticosteroids after 3–5 days, rescue therapy with cyclosporine or infliximab should be initiated. However, surgery should be considered if all the medical treatments are unsuccessful.[140,141]

Statement 5.4.2
ASUC is defined as a bloody stool ≥6 times/day with at least one of the following: pulse rate >90 bpm, temperature >37.8°C, hemoglobin <10.5 g/dL, erythrocyte sedimentation rate (ESR) >30 mm/hr, or CRP >3 mg/dL.

It is crucial to distinguish between patients with mild or moderately to severely active disease who can be managed as outpatients and those with ASUC requiring hospitalization. According to the Truelove and Witts criteria, patients with ASUC are characterized by bloody stool frequency of ≥6/day and tachycardia (>90 bpm), fever (>37.8°C), anemia (hemoglobin <10.5 g/dL), elevated ESR (>30 mm/hr), and elevated CRP level (>30 mg/L).[40,101] For pediatric patients, a PUCAI at least 65 is diagnostic of ASUC.[96]

Statement 5.4.3
Infections, especially *C. difficile* and CMV, need to be ruled out during every acute flare-up of patients with UC.

It is crucial to rapidly identify, closely monitor and promptly reassess ASUC treatment. Hospitalization is mandatory for patients meeting the ASUC criteria. Stool tastings for enteric pathogens and *C. difficile* should be obtained promptly, but results should not be awaited before rapid IV corticosteroid therapy. The diagnosis should be confirmed, and CMV infection should be excluded through flexible unprepared sigmoidoscopy with minimal air insufflation.[142] CMV reactivation can occur in immunosuppressed patients with severe UC and may lead to refractory or severe relapses. Therefore, CMV infection should be ruled out in patients who experience relapses while receiving immunosuppressive therapy.

Statement 5.4.4
The first-line treatment for ASUC is IV corticosteroids. The optimal treatment duration for IV corticosteroids is 5–7 days. When with an unsatisfactory response on the 3rd day after initiating standard dosage IV steroid, early consultation with a surgeon should not be delayed.

For pediatric patients, IV methylprednisolone at 1 mg/kg/day, with a maximum dosage of 40 mg/day, is preferred because of its fewer mineralocorticoid effects than hydrocortisone.[143] For adult patients, the recommended treatment options include IV hydrocortisone at 100 mg four times daily and IV methylprednisolone at 40–60 mg. However, over 7–10 days of IV corticosteroid treatment showed no benefit in this population. Early and multidisciplinary planning of medical and/or surgical rescue therapy for nonresponsive patients was shown to decrease ASUC mortality.[142,144]

Following hospitalization, IV corticosteroid treatment should be continued for 2–3 days, and physicians should evaluate symptoms daily, including stool frequency, urgency, bleeding, and abdominal pain and/or fullness. Furthermore, it is critical to clinically assess patients for severe abdominal pain, which indicates ASUC instability. When severe abdominal pain persists, peritoneal signs should be closely monitored, and patients should undergo an X-ray examination as needed.[127,141] Patients who have a toxic megacolon, which is characterized by a colon dilation greater than 6 cm along with systemic symptoms, are at high risk for colon perforation. These patients should be promptly referred to a surgeon for an emergency colectomy.

Additionally, inflammatory markers such as CRP and albumin should be evaluated daily to ensure the efficacy of IV corticosteroid treatment. The TACOS trial investigated tofacitinib plus corticosteroids for treating ASUC, involving 104 randomized patients.[145] Results demonstrated that tofacitinib increased

the response rates to 83% compared to 59% in the steroid-only group and reduced the necessity for rescue therapy. The study recommends tofacitinib while continuing IV corticosteroids as an effective addition to ASUC treatment, with predominantly mild side effects, except for a single incident of serious thrombosis.

Statement 5.4.5
The second-line treatment for ASUC after the failure of first-line IV corticosteroid treatment includes infliximab, calcineurin inhibitors (including cyclosporine and tacrolimus), or emergency colectomy.

When there is no significant symptom improvement by days 3–5 according to the Oxford and Lichtiger scores, the use of second-line therapy should be considered. However, it is crucial to carefully evaluate the patient's symptoms and not delay colectomy if required. Infliximab, cyclosporine, and tacrolimus are the leading second-line therapy options for patients with ASUC who do not respond to IV corticosteroid treatment.

Infliximab was proven to effectively reduce the need for colectomy.[146] Currently, there is no consensus on whether to use a standard dose (5 mg/kg) or a high dose (10 mg/kg) of infliximab induction regimen.[147] In some retrospective studies, the higher-dose regimen did not achieve a significant reduction in the rate of short-term colectomy.[148,149] In a retrospective cohort study of 50 patients with ASUC, the rate of colectomy during induction therapy was significantly lower with the accelerated regimen (6.7%, 1/15 patients) than with the standard regimen (40%, 14/35 patients) (P=0.039).[150] However, these studies are often retrospective and small-scale and involve patients with more severe UC who are in high-dose or accelerated infliximab induction.

Cyclosporine, a calcineurin inhibitor with rapid onset and short half-life, is considered an alternate treatment in patients with ASUC contraindicated for corticosteroids or as the long-term bridge treatment between IV corticosteroids and AZA.[146] A randomized controlled trial suggested that cyclosporine at 2 mg/kg/day had a clinical response rate similar to cyclosporine at 4 mg/kg/day in patients with ASUC but with a better safety profile.[151]

Regarding tacrolimus, Komaki et al.[152] conducted a systematic review and meta-analysis of 2 randomized controlled trials and 23 observational studies to compare tacrolimus to placebo as rescue therapy in patients with ASUC refractory to corticosteroids. They found that patients given tacrolimus showed greater clinical responses within 2 weeks than those given the placebo in randomized controlled trials (RR, 4.61; 95% CI, 2.09–10.17).[141,146]

According to CONSTRUCT[153] and CYSIF trials,[154] no significant differences were found between cyclosporine and infliximab regarding treatment failure rate (risk difference 6%; 95% CI: −7–19; P=0.52), survival rate (mean adjusted difference 7.9; 95% CI: −22.0–37.8; P=0.60), and mean time to colectomy (811 days vs. 744 days: 95% CI, 707–912 days in the infliximab group vs. 638–850 days in the cyclosporine group, respectively, P=0.25). A meta-analysis revealed that infliximab is associated with reduced colectomy rate in the short-term and at 1 year, and there is a tendency for a lower 3-year colectomy rate compared to cyclosporine.[155] However, no significant difference was noted in efficacy between infliximab and tacrolimus.

Evidence regarding the effectiveness of other second-line treatments for ASUC is limited, and a consensus on the choice of third-line therapies is unclear.[141,146] In the REASUC study,[156] a retrospective analysis of 78 patients who received infliximab, cyclosporine, tofacitinib, and ustekinumab as third-line therapy, colectomy was performed in 29 patients (37%) during the median follow-up of 21 weeks. At 12 and 52 weeks, 32 and 18 patients were in clinical remission, respectively. Two patients (2.6%) died, including one following colectomy. Short-term risk factors for colectomy included older age at hospital admission (OR, 1.1; 95% CI, 1.0–1.1), the use of cyclosporine as third-line salvage therapy (OR, 8.0; 95% CI, 1.3–48.5), and severe disease. Therefore, colectomy remains the standard treatment for third-line therapy. Alternatively, patients may seek further treatment at specialized centers for IBD to explore the use of other medications.

6. Treatment Targets and Disease Monitoring

Statement 6.1
Patient-reported outcomes (PROs) are short-term treatment targets associated with patient well-being. Level of agreement: Strongly agree, 70.0%; agree, 30.0%; disagree, 0.0%.

PROs are standardized instruments that measure patients' perceptions of their symptoms, functional abilities, mental well-being, and overall QoL, among other aspects of their daily experiences. Initially designed for research, PROs are increasingly utilized in clinical practice to enable healthcare providers to assess symptom severity and diverse health outcomes from the patient's perspective. PRO2 has become the standard for assessing UC symptoms, comprising stool frequency and

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rectal bleeding from the Mayo score. The correlation between PRO2 and EH was moderate to high.[104,157] Additionally, PROs have been shown to correlate with noninvasive biomarkers such as FC to assess disease control in UC patients. Marcovitch et al.[158] developed and validated TUMMY-UC, a PRO measure designed explicitly for pediatric UC patients.[144] They demonstrated that TUMMY-UC is a reliable, valid, and responsive PRO measure for examining disease activity in pediatric UC patients.[158] Overall, PROs are crucial in assessing symptoms and QoL in patients with UC, and further research is warranted to develop more comprehensive and patient-centered measures.[157]

Statement 6.2
Biomarkers. Level of agreement: Strongly agree, 63.3%; agree, 36.7%; disagree, 0.0%.

Statement 6.2.1
FC is a sensitive, noninvasive biomarker for correlating to endoscopic indices, assessing disease activity, and detecting relapse in patients with UC.

FC is a noninvasive and more sensitive biomarker for predicting endoscopic activity in UC patients than CRP and ESR. It is stable in feces and specific to the gut and released by white blood cells in response to inflammation in the intestinal mucosa. Conversely, CRP and ESR are general markers of inflammation and can be elevated in response to inflammation in other parts of the body. Further, FC levels correlate more strongly with endoscopic activity in UC than CRP and ESR.[104,159] Schoepfer et al.[160] found that the accuracy for detecting active disease endoscopically was higher for FC (89%) than for the Clinical Activity Index (73%), CRP (62%), and leukocytosis (60%). While FC is valuable for evaluating disease activity and response to therapy in IBD, its specificity is limited. It does not reliably distinguish among various etiologies of gut inflammation, including infectious gastroenteritis, malignancies, eosinophilic colitis, lymphocytic colitis, and celiac disease.[161-163]

Statement 6.2.2
CRP and ESR can serve as adjunctive markers for assessing treatment response in UC.

CRP and ESR are noninvasive biomarkers that can be used as adjunctive measures to investigate treatment response in UC. CRP is an acute-phase protein synthesized by the liver in response to inflammation.[149,150] Elevated CRP levels have been associated with severe clinical activity, anemia, hypoalbuminemia, and active disease on endoscopy in UC patients.[149,150] Contrastingly, the ESR reflects the rate at which red blood cells settle in a test tube over time. Elevated ESR levels have further been associated with active UC disease. As regards mechanism, CRP and ESR levels are believed to reflect the degree of inflammation in the body and, therefore, can be used as surrogate markers of disease activity in UC. However, CRP and ESR should not be used alone as treatment targets since they have inadequate operational characteristics to act as surrogates for endoscopic, radiographic, or clinical endpoints.[164,165]

Statement 6.3
IUS can be used to monitor disease activity and treatment response. Level of agreement: Strongly agree, 33.3%; agree, 60.0%; disagree, 6.7%.

Studies have shown that IUS can be used to monitor treatment response in UC patients.[166-168] A retrospective study found a statistically significant correlation between BWT and the MES ($r=0.434$, $P=0.010$) and the Geboes index ($r=0.298$, $P=0.027$) by both IUS and colonoscopy.[166] A prospective, longitudinal cohort study that used IUS to monitor tofacitinib treatment response in patients with moderate to severe UC (MES ≥2) showed that IUS, particularly BWT, was more accurate in detecting segmental endoscopic remission, improvement, and response than globally used endoscopic scoring indices. This indicates that IUS, particularly BWT, can be a reliable and accurate tool for investigating endoscopic remission and response in UC patients.[167] Furthermore, the TRUST&UC study proposed IUS as a point-of-care tool to monitor the disease trajectory and short-term response to treatment in UC patients.[168] Despite its value in assessing disease activity in UC, the interrater reliability was fair, and further research and validation are required to confirm these findings.[104]

Statement 6.4
Endoscopy. Level of agreement: Strongly agree, 63.3%; agree, 36.7%; disagree, 0.0%.

Statement 6.4.1
Endoscopic remission in UC is associated with improved long-term clinical outcomes.

EH refers to the complete healing of the mucosal lining of the intestines. It is a crucial goal in IBD treatment. Achieving EH is essential in preventing complications from mucosal inflammation and improving outcomes in IBD patients. The healing of the mucosal lining in UC patients is associated with a lower

risk of colectomy and disease relapse and improved long-term remission rates.[169,170] The standard endoscopic scores for UC include the MES and UC Endoscopic Index of Severity, which are commonly used in clinical trials and practice to assess the degree of inflammation in UC patients. EH, defined as an MES of 0 or 1, is a long-term treatment target in UC. Complete EH, defined as an MES of 0, is associated with superior disease outcomes.[104] However, defining the best time for reassessing mucosal healing is challenging, although it can be predicted from clinical trial data. Mucosal healing could be determined about 3–6 months after treatment initiation in patients showing clinical responses to treatment to avoid poor treatment outcomes caused by delayed endoscopic evaluation.[43,171]

Statement 6.4.2
Endoscopic reassessment should be considered in cases of relapse, refractoriness, the development of new symptoms, or when surgical intervention or changing therapy is indicated.

Endoscopic reassessment to determine whether the treatment effectively promotes mucosal healing and reduces inflammation. Moreover, it is crucial to identify changes in disease extent and activity. When patients receiving treatment show no improvement in their condition, endoscopic reassessment should be considered in case of relapse, persistent disease activity, or new symptom development and to change the therapy strategy for more effective treatment. However, given the risk of bowel perforation, full colonoscopy is typically not recommended for patients with ASUC. Instead, flexible sigmoidoscopy is recommended to be performed cautiously when determining disease activity and identifying whether patients have superimposed colitis, including CMV, *C. difficile*, or ischemic colitis.[40,46]

Statement 6.5
Achieving histological remission is valuable in predicting long-term remission and preventing cancer development. The Nancy index is a simplified histological score for monitoring histologic activity. Level of agreement: Strongly agree, 63.3%; agree, 36.7%; disagree, 0.0%.

Histologic remission refers to the absence of inflammation in the tissue lining the colon and is valuable in predicting long-term remission and preventing cancer development. However, achieving this goal is challenging.[104,172] In the ACT trials, only one-third of patients achieved both mucosal healing and histologic remission, emphasizing the difficulty in attaining this outcome.[120] Different scoring systems are used to evaluate disease activity and inflammatory status in UC patients. The MES and histologic scores show a statistically significant overall correlation (the highest being Kendall's $\tau = 0.482$, $P < 0.0001$). However, this correlation is significant only for the extreme groups, including those in remission and with severe disease, with misclassifications observed for mild disease.[173] However, histologic healing currently has limited clinical utility owing to a lack of standardized reporting methods.[104,174,175]

7. Surgery

Statement 7.1
Life-threatening conditions (e.g., bowel perforation, massive bleeding, toxic megacolon, and fulminant colitis refractory to medical treatment) are indications for emergent surgery. Persistent symptoms or intolerable side effects related to medical treatment, high-grade dysplasia, or carcinoma are indications for elective surgery. Level of agreement: Strongly agree, 80.0%; agree, 20.0%; disagree, 0.0%.

The timing of surgery varies depending on the severity of the patient's condition. For those with ASUC, immediate surgical consultation and collaborative care are strongly advised. In life-threatening situations, emergency surgical intervention is critical.[176-178] Patients with UC and high-grade dysplasia are at increased CRC risk. Elective surgery is recommended in such cases. However, current evidence is insufficient to determine whether low-grade dysplasia requires surgical intervention. Nonetheless, it is crucial to continue surveillance for those patients.[176,179] Moreover, elective surgery can be considered for patients who experience significant side effects from medications or whose symptoms persist despite treatment. The surgery decision depends on each patient's condition and preference and should consider their specific benefits and risks.[180]

Statement 7.2
Preoperative conditions, including nutrition status, immunosuppressant use, and overall performance, should be optimized before surgery. Weaning of steroid as possible should be considered for patients who are under high-dose steroid therapy. Level of agreement: Strongly agree, 66.7%; agree, 33.3%; disagree, 0.0%.

Patients taking > 20 mg of prednisolone for more than 6 weeks are at increased risk of short-term pouch-specific complications during surgery.[40,181] Since corticosteroids suppress the immune system, they make patients more susceptible to in-

https://doi.org/10.5217/ir.2023.00050 • Intest Res 2024;22(3):213-249

fections. Furthermore, prolonged use of high-dose corticosteroids may hinder the healing of wounds and elevate the risk of infections after surgery. Therefore, steroids should be weaned before surgery; otherwise, the surgery should be postponed to reduce the risk of infection and complications. Additionally, patients receiving biologics, such as anti-TNF, are at increased risk of developing early and late pouch-specific complications.[181] In contrast, the use of thiopurines or cyclosporine before surgery does not increase the risk of postoperative complications.[181] However, these observations are based on low-quality evidence.[40,181] Moreover, lower preoperative body mass index, hemoglobin levels, serum albumin levels, and pancolitis were associated with reoperation.[182] Therefore, pre-operation optimization of the patient's condition is vital to decrease operation-related morbidities.

Statement 7.3
The 3-stage procedure is probably safer for high-risk patients, such as those with severe colitis; on preoperative biologics, immunomodulators, or high-dose steroids; with malnourishment; or with anemia. The timing of pouch creation should be tailored to each patient based on their history and presentation, as well as the surgeon's expertise. Level of agreement: Strongly agree, 46.7%; agree, 53.3%; disagree, 0.0%.

Depending on the patient's characteristics, various surgical procedures may be considered. The differences among them include resecting the entire colon with or without the rectum, the type of gastrointestinal reconstruction, and deciding between a permanent and reversible ileostomy.[183] For patients with colitis requiring surgery, minimally invasive procedures (e.g., laparoscopic surgeries) may offer short-term advantages compared to open colectomy.[184,185] For patients at risk of postoperative complications, a 3-stage procedure is recommended. The 3-stage procedure involves subtotal colectomy with end ileostomy at the first operation, followed by ileal pouch-anal anastomosis (IPAA) and stoma closure. However, the modified 2-stage IPAA may also be considered owing to its association with lower anastomotic leakage rates, lower resource consumption, and shorter hospital stays.[186,187] Mège et al.[188] indicated that the 3-stage laparoscopic IPAA had similar postoperative morbidity with the 2-stage procedure but was more frequently performed in patients with acute colitis. Therefore, the 3-stage procedure was advantageous for high-risk patients. A prospective randomized trial demonstrated that early closure (7–12 days) of a diverting ileostomy in patients undergoing IPAA was associated with higher complication rates and more severe complications than late closure (≥8 weeks).[189] Surgeons' experience and the patient's characteristics should be considered when deciding on the appropriate operative plan.[189,190]

Statement 7.4
Total colectomy with ileorectal anastomosis (IRA) could be an option in selected patients with UC and relative rectal sparing. Regular surveillance of the rectum is mandatory due to the potential risk of cancer. Level of agreement: Strongly agree, 56.7%; agree, 43.3%; disagree, 0.0%.

The use of total abdominal colectomy with an initial or staged IRA is a viable option for patients with UC. This approach offers comparable QoL and functional outcomes to an IPAA.[176,191] For females, this option is beneficial since it avoids pelvic dissection and may preserve fertility.[192-194] However, patients receiving IRA for UC remain at risk of developing rectal carcinoma, making long-term surveillance of the rectum essential. The estimated incidence of rectal carcinoma after IRA for UC is 3.2% at 10 years and 7.3% at 20 years.[195] Additionally, patients who choose IRA as their primary reconstruction do not have a higher risk of failure for a later secondary IPAA than those who undergo IPAA initially. The 10-year pouch survival rate was estimated to be 94% (95% CI, 93%–96%) for primary and 92% (95% CI, 81%–97%) for secondary IPAA.[196] In high-risk patients, such as those with primary sclerosing cholangitis (PSC) or prior colonic neoplasia, IPAA or end ileostomy should be considered.[195,196]

8. Special Groups Consideration

Statement 8.1
Maintaining remission is associated with better pregnancy outcomes. A multidisciplinary team care with preconception consultation is suggested. Level of agreement: Strongly agree, 86.7%; agree, 13.3%; disagree, 0.0%.

Female IBD patients often have concerns about the potential impact of pregnancy on the progression of their disease, and the potential consequences of the disease and medications they are prescribed for the fetus. While pregnancy has minimal effects on IBD in most females, it is estimated that around 30% with UC may experience a disease flare during pregnancy.[197] These flares are more common in the first trimester and during delivery. An ongoing inflammatory condition may adversely affect pregnancy and the fetus, potentially leading to

premature birth, lower birth weights, and, in severe cases, fetal loss. Hence, planning for pregnancy is recommended when the disease is in remission.[197]

Statement 8.2
Most conventional and biological agents could be maintained during pregnancy, except small molecules. Level of agreement: Strongly agree, 50.0%; agree, 50.0%; disagree, 0.0%.

Medications to treat IBD during pregnancy should be used to maintain disease remission, rather than discontinue the medications because of the concerns about potential harm to the fetus. Real-world data suggests that the majority of medications are safe for use during pregnancy, as clinical trials typically do not include pregnant individuals. Aminosalicylates (e.g., sulfasalazine and mesalazine) can be continued; however, sulfasalazine interferes with folic acid synthesis, and pregnant females should take a higher folic acid dose for supplementation.[198] Using steroids may increase the risk of maternofetal adverse events; however, they provide benefits for disease control.[199] Thiopurines, such as AZA and 6-MP, are safe during pregnancy since recent studies have found no increased risk of congenital abnormalities or pregnancy complications.[200,201] The use of calcineurin inhibitors, such as cyclosporine, during pregnancy is associated with potential risks such as hypertension, gestational diabetes, preterm birth, low birth weight, and small for gestational age.[202] Therefore, cyclosporine was recommended as salvage therapy by the AGA.[203]

Anti-TNF agent use during pregnancy has not shown increased adverse fetal outcomes.[203-205] Data from the Pregnancy Inflammatory Bowel Disease and Neonatal Outcomes registry from 1,669 completed pregnancies revealed no increased risks of major pregnancy or neonatal complications with ustekinumab or vedolizumab exposure.[206] Therapy with these agents can be continued throughout pregnancy in females with IBD to maintain disease control and reduce pregnancy-related adverse events.[206] AGA recommends continuing dosing throughout the first to third trimesters and planning the final dose according to the drug half-life to minimize placental transfer.[203]

Tofacitinib has shown teratogenic effects in animal studies, but minimal clinical data is available.[198] It is recommended to consider other treatment options and avoid using tofacitinib, particularly in the first trimester of pregnancy. The use of filgotinib and ozanimod during pregnancy is contraindicated since filgotinib may cause fetal harm, and human data is lacking for ozanimod.[198,207] While no human studies have confirmed the safety of upadacitinib during pregnancy, animal studies have indicated teratogenic effects. Therefore, the product labeling advises against using upadacitinib during pregnancy.[208] Regarding breastfeeding, most medications prescribed for IBD are considered safe, except for metronidazole and rifaximin, which should be avoided for lactating mothers.[198]

Statement 8.3
For pediatric patients, long-term corticosteroid should be avoided. Level of agreement: Strongly agree, 86.7%; agree, 13.3%; disagree, 0.0%.

While corticosteroids are effective and can help achieve clinical remission in children with IBD, long-term treatment has some limitations, such as adrenal suppression, growth impairment, delayed puberty, decreased bone mineral density, and behavioral effects.[193] The goal of IBD treatment in children is to eliminate symptoms, restore QoL, minimize the adverse effects of medications, and prevent complications. Inducing remission of active disease and maintaining remission in children with quiescent disease are also crucial factors to consider. Budesonide is a topically acting corticosteroid that can reduce adverse effects due to substantial first-pass hepatic metabolism, making it suitable for use in children with mild to moderate IBD.[209,210]

Statement 8.4
For pediatric patients with moderate to severe UC who failed conventional agents, infliximab and adalimumab could be considered. Level of agreement: Strongly agree, 53.3%; agree, 46.7%; disagree, 0.0%.

Anti-TNF agents are commonly recommended for children with IBD who do not respond to or are dependent on corticosteroids. Hyams et al.[211] reported that infliximab showed a 73% response rate at week 8 and a 29% remission rate at week 54, leading to its approval by the U.S. Food and Drug Administration (FDA) to treat children with moderately to severely active UC. The ENVISION I study assessed the safety and efficacy of adalimumab in children with moderate to severe UC.[196] Its results revealed a remission rate of 53% at week 8 and 37% at week 52.[212] The most common adverse events reported were headache and anemia.[212] Biologics or small molecules such as golimumab, vedolizumab, ustekinumab, tofacitinib, and upadacitinib have not been approved by the FDA to treat children with UC; however, studies are ongoing to evaluate their efficacy and safety in those who do not respond to conventional therapy.[213-217]

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Statement 8.5
Since polypharmacy and comorbidities are common in elder patients, concomitant infection and drug interactions should be taken into consideration. Level of agreement: Strongly agree, 93.3%; agree, 6.7%; disagree, 0.0%.

The incidence of IBD among elder patients is increasing globally. There are similarities but also differences in clinical features and treatment options for older compared to younger IBD patients.[218] The incidence and severity of major UC symptoms, including bleeding, diarrhea, abdominal pain, weight loss, and fever, differ between elder and younger patients.[219] The compromised immune systems of older patients increase their vulnerability to infectious diseases, particularly when they receive corticosteroid or immunosuppressive drug treatments. Elderly UC patients had a higher risk of HZ with tofacitinib treatment.[219] Thus, healthcare providers should consider comorbidities, susceptibility to infection, and cancer risk when deciding on medical treatments for elder UC patients.[219,220]

Statement 8.6
Adequate disease control is as important in elder patients as the younger patients to decrease the UC related complications. Level of agreement: Strongly agree, 66.7%; agree, 33.3%; disagree, 0.0%.

The response rates with corticosteroids and aminosalicylates were similar in elder and younger IBD patients.[221] Additionally, no differences in efficacy have been noted with thiopurines.[221] Treatment for UC is generally consistent between older and younger patients. However, older IBD patients often manage complex medication regimens, increasing the risk of interactions and toxicity. An older patient's frailty and overall health should be examined when considering treatments. Less aggressive therapy and suboptimal disease management, along with conservative medication use, may lead to higher surgery and mortality rates in elderly IBD patients.[221,222] Therefore, adequate disease control is equally important in elderly and younger patients.

9. CRC Surveillance

Statement 9.1
Since patients with UC are at increased risk of developing CRC, disease control and regular surveillance are essential. Level of agreement: Strongly agree, 90.0%; agree, 10.0%; disagree, 0.0%.

Patients with IBD have a heightened risk of developing CRC.[223,224] In Taiwan, the incidence of CRC is higher among patients with UC than in the general population, predominantly in males.[6,16,32,225]

While successful endoscopic dysplasia resection reduces CRC risk, continued surveillance remains critical since IBD patients are at risk for metachronous neoplasia.[226,227] Interestingly, the excess risk of CRC in IBD patients has declined in several regions, possibly due to improved surveillance methods and better inflammation management.[228] However, cases with early CRC have increased, which may be attributed to a shift from surgical management to endoscopic resection of dysplasia.[228]

Statement 9.2
Colonoscopic surveillance for dysplasia should be offered to all patients 8 years after the onset of UC. Those with concurrent PSC should receive a colonoscopy immediately, and annual surveillance is recommended. Level of agreement: Strongly agree, 66.7%; agree, 33.3%; disagree, 0.0%.

Owing to the increased risk of CRC in IBD patients and mucosal dysplasia, conducting surveillance colonoscopy to reduce the incidence of CRC is crucial.[40] Various guidelines recommend different surveillance intervals based on the patient's risk level.[43,100,229] For example, the ACG recommends conducting surveillance colonoscopies every 1–3 years,[100] and the Japanese Society of Gastroenterology recommends surveillance every 1–2 years.[229] Both guidelines propose performing endoscopic monitoring 8 years after UC diagnosis. The ECCO guidelines recommend scheduling subsequent surveillance annually for high-risk patients, 2–3 years for intermediate-risk patients, and 5 years for low-risk patients.[43] However, patients co-diagnosed with PSC should immediately undergo colonoscopy, and annual surveillance is advised.[40]

Risk factors of advanced colorectal neoplasia in IBD patients include extensive colonic disease, post-inflammatory polyps, colonic strictures, and histologic inflammation severity.[228] However, creating a practical score for cumulative inflammation that can be used in routine practice remains challenging.[228] Studies have indicated low adherence to surveillance guidelines among eligible IBD patients.[230,231] In the CESAME cohort survey, only 54% of eligible French patients received at least one surveillance colonoscopy during a 7-year period.[230] Another regional UK-based study showed that almost two-thirds of eligible patients with IBD-associated CRC were not under surveillance.[231] The studies underscore the low adher-

ence to surveillance guidelines among IBD patients, potentially due to perceived low cancer risk, intolerance to bowel preparation, and various patient-related factors affecting surveillance uptake.[226]

Statement 9.3
The surveillance technique. Level of agreement: Strongly agree, 33.3%; agree, 66.7%; disagree, 0.0%.

Statement 9.3.1
High-definition colonoscopy with targeted biopsies is recommended for surveillance. Random biopsies could be performed in some special cases, such as in PSC, lead pipe colon, and previous dysplasia areas.

Statement 9.3.2
Dye spray chromoendoscopy (DCE) is preferred over white-light standard colonoscopy. Virtual chromoendoscopy (VCE) could be an alternative to DCE to detect dysplasia while using a high-definition colonoscope.

The recommended approach for detecting dysplasia in IBD patients includes both targeted and nontargeted biopsies. The traditional approach to IBD surveillance colonoscopy involves quadrantic nontargeted colonic biopsies, which are time-consuming and more costly.[227,232] Both DCE and VCE can enhance the visibility of dysplastic lesions by highlighting their borders and surface architecture, resulting in a higher dysplasia detection rate. These methods should be particularly considered if a standard-definition endoscope is used or if there is a history of dysplasia.[227] The VIRTUOSO trial[232] revealed that the use of high-definition colonoscope showed similar dysplasia detection rate when using targeted biopsies and nontargeted biopsies. Nontargeted biopsies are not routinely required with the use of high-definition endoscopes. However, they should be considered for patients with a history of neoplasia, concomitant PSC, or a tubular colon.[227] Adequate bowel preparation, careful washing and inspection of all colorectal mucosa, and targeted sampling of any suspicious mucosa are warranted for colonoscopy surveillance.

Statement 9.4
When dysplasia in UC is endoscopically resectable, endoscopic resection could be considered. However, subsequent surveillance at adequate interval should be performed. Level of agreement: Strongly agree, 63.3%; agree, 36.7%; disagree, 0.0%.

The "five S" features describe colonic lesions including their shape, size, site, surface (Kudo pit pattern), and surrounding (mucosal activity and other lesions). This provides a detailed and systematic approach to characterizing colonic lesions.[233] Physicians can use these features to determine appropriate treatments, such as endoscopic resection or surgery. A multicenter study from Japan included 336 UC patients and assessed the efficacy and safety of endoscopic resection in 199 patients versus surgery in 137 patients for colorectal neoplasms, over a follow-up period of 34.7 months.[234] The study reported a 2.5% perforation rate, 2.7% local recurrence rate, and 6.1% metachronous neoplasia rate in the endoscopic resection group, with a significantly higher overall survival rate compared to surgical cases ($P=0.009$).[234] A meta-analysis of 11 studies found a complete endoscopic resection resection rate of 97.9% from 610 lesions. The local recurrence rate was 4.9%, and metachronous lesions occurred in 7.4% of patients, and 0.2% of metachronous colon cancer was detected over a median follow-up of 33 months.[235] Thus, continuous post-treatment surveillance is crucial to detect any subsequent neoplastic developments following endoscopic resection.[227,234]

Statement 9.5
When dysplasia in UC is high-grade, multifocal or endoscopically unresectable, surgical consultation is recommended. Level of agreement: Strongly agree, 73.3%; agree, 26.7%; disagree, 0.0%.

Owing to the high risk of colorectal dysplasia in IBD patients, until recently, guidelines still recommended proctocolectomy for IBD patients, including those with UC.[228] Currently, endoscopic methods are increasingly preferred for treating dysplastic lesions; however, surgical consultation is recommended for those that are unresectable because of size, location, signs of invasive cancer, or submucosal fibrosis.[227] Notably, surgical consultation should be made based on the individual situation and specific circumstances of the patient.[227,228]

CONCLUSIONS

The expert panel convened by TSIBD meticulously established these consensus statements on diagnosing and managing UC in Taiwan. The panel considered available evidence and expert opinions through a rigorous process involving thorough discussions and voting. The recommendations were tailored to the unique medical environment of Taiwan, considering factors such as endemic diseases, treatment availability, and NHI coverage (Table 5). The recommended treatment algo-

https://doi.org/10.5217/ir.2023.00050 • Intest Res 2024;22(3):213-249

Table 5. The Taiwan Society of Inflammatory Bowel Disease Consensus Guidelines for UC Updated in 2023

1. Epidemiology
1.1 The incidence and prevalence of UC in Taiwan are increasing, but this number is still underestimated.
1.2 In Taiwan, similar to other Eastern Asian countries but in contrast to Western countries, UC is more common in men.
1.3 In Taiwan, the prevalence of EIMs ranges from 2.8% to 26.6% in patients with UC.
2. Diagnosis
2.1 The diagnosis of UC is based on medical history, clinical evaluation, and endoscopic and histological findings, especially after the exclusion of infectious etiologies.
2.2 A comprehensive medical history of UC and EIMs should be assessed. The most common symptoms include diarrhea, blood/mucus in stool, and/or rectal urgency.
2.3 Investigations at diagnosis include markers of disease activity and nutrition status and exclude gastrointestinal infection.
2.4 Colonoscopy is the mainstay for evaluating UC. The typical endoscopic feature of UC is diffuse, continuous inflammation (loss of vascular pattern, granularity, friability, and ulceration) involving the rectum with or without proximal extension into the colon.
2.5 Endoscopic findings may be atypical, especially in treatment-experienced patients with UC.
2.6 Abdominal radiography is recommended for patients with suspected ASUC to detect toxic megacolon. Computed tomography could be indicated to identify complications.
2.7 IUS can be used to assess disease extent and severity in patients with UC.
2.8 The histological diagnosis of UC is based on 2 main components in the lesions: architectural change and inflammatory status.
2.9 The major role of pathology in diagnosing UC is to exclude other etiologies, such as infection, malignancy, etc.
3. Specific Considerations
3.1 HBsAg, anti-HBs, and anti-HBc should be routinely checked before treatment initiation, especially before the initiation of immunomodulators, steroids, and advanced therapy.
3.2 In patients who are HBsAg and/or anti-HBc positive, HBV DNA quantification is recommended before the initiation of steroids, immunomodulators, biologics, and small molecules.
3.3 In patients positive for HBsAg and/or with detectable HBV DNA, preventing HBV reactivation should be considered.
3.4 Screening for TB infection with chest radiography and IGRA assays or TST is recommended before initiating advanced therapy in patients with UC.
3.5 In patients diagnosed with LTB, prophylactic treatment to prevent TB reactivation should be started at least 4 weeks before using advanced therapy.
3.6 During advanced therapy, patients should be monitored for signs and symptoms of active TB with chest X-ray and IGRA or TST performed at least annually.
3.7 Vaccination before starting immunosuppressive treatment
3.7.1 HBV vaccination is recommended in patients who are negative for HBsAg, anti-HBs, and anti-HBc.
3.7.2 Herpes zoster vaccine is recommended for patients before immunosuppressive therapy, or at least for immunocompetent patients aged more than 50 years.
3.7.3 Human papillomavirus vaccination is recommended for patients younger than 26 years old.
4. Evaluation and Treatment Goals
4.1 Clinical classification (Montreal classification) and activity scores (Mayo score for adults and Pediatric UC Activity Index for children) are recommended for the assessment of patients with UC.
4.2 Macro- and micronutrient deficiencies are prevalent in patients with UC. Adequate nutritional assessment, monitoring, and support are recommended.
4.3 The treatment of UC depends on the severity and extent of disease. The goals of treatment include induction and maintenance of remission, prevention of complications, and improving quality of life.
5. Treatment
5.1 Nutrition
5.1.1 EN appears safe, and PN is recommended for patients with UC when they cannot tolerate EN or its associated complications such as toxic megacolon, etc.
5.1.2 All patients with UC should undergo counseling by a dietician as part of the multidisciplinary approach to improve nutritional therapy and avoid malnutrition and nutrition-related complications.

(Continued to the next page)

Table 5. Continued

5.2 Conventional therapy
5.2.1 Induction of remission in patients with mild to moderate UC.
5.2.1.1 For patients with mildly active ulcerative proctitis, topical 5-ASA therapies at a dose of 1 g/day is recommended to induce remission.
5.2.1.2 For patients with mildly to moderately active left-sided UC, a combination of topical 5-ASA at a dose of at least 1 g/day and oral 5-ASA at a dose of at least 2 g/day is recommended.
5.2.1.3 For patients with mildly to moderately active extensive colitis, oral 5-ASA at a dose of at least 2 g/day with supp/enema is recommended to induce remission.
5.2.2 For patients with mildly to moderately active UC not responding to 5-ASA, we recommend adding budesonide MMX at a dose of 9 mg/day to induce remission.
5.2.3 Induction of remission in patients with moderate to severe UC
5.2.3.1 For patients with mild to moderate UC who fail 5-ASA and/or budesonide MMX induction and those with moderate to severe UC, we recommend systemic corticosteroids to induce remission.
5.2.3.2 For patients with severe UC, IV corticosteroids is recommended.
5.2.4 Maintenance of remission in patients with mild to moderate UC
5.2.4.1 For patients who previously responded to 5-ASA induction treatment, retaining 5-ASA treatment as the maintenance therapy is recommended.
5.2.4.2 Steroid free is the goal of long-term treatment. Therefore, we recommend against corticosteroids for maintenance of remission in pat ients with UC.
5.2.4.3 For patients with steroid dependence, we suggest bridging to thiopurine or advanced therapies for maintenance of remission.
5.2.4.4 Patients with steroid- or immunomodulator-refractory disease should be treated with advanced therapies or tacrolimus.
5.3 Advanced therapy
5.3.1.1 Anti-tumor necrosis factor agents (infliximab, adalimumab, and golimumab) are recommended for induction and maintenance of remission in patients with moderately to severely active UC.
5.3.1.2 When infliximab is used for patients with moderately to severely active UC, combination with thiopurine is suggested.
5.3.2 Vedolizumab is recommended for induction and maintenance of remission in patients with moderately to severely active UC.
5.3.3 Antibodies targeting interleukin-12/23 (ustekinumab) or interleukin-23 (mirikizumab) are recommended for induction and maintenance of remission in patients with moderately to severely active UC.
5.3.4 Janus kinase inhibitors (tofacitinib, upadacitinib, and filgotinib) are recommended for induction and maintenance of remission in patients with moderately to severely active UC.
5.3.5 Ozanimod is recommended for induction and maintenance of remission in patients with moderately to severely active UC.
5.4 Management of ASUC
5.4.1 Approximately 20%–25% of patients with UC experience at least one severe acute exacerbation, often necessitating hospitalization, throughout their disease journey.
5.4.2 ASUC is defined as a bloody stool ≥ 6 times/day with at least one of the following: pulse rate > 90 bpm, temperature > 37.8°C, hemoglobin < 10.5 g/dL, ESR > 30 mm/hr, or CRP > 3 mg/dL.
5.4.3 Infections, especially *Clostridium difficile* and cytomegalovirus, need to be ruled out during every acute flare-up of patients with UC.
5.4.4 The first-line treatment for ASUC is IV corticosteroids. The optimal treatment duration for IV corticosteroids is 5–7 days. When with an unsatisfactory response on the 3rd day after initiating standard dosage IV steroid, early consultation with a surgeon should not be delayed.
5.4.5 The second-line treatment for ASUC after the failure of first-line IV corticosteroid treatment includes infliximab, calcineurin inhibitors (including cyclosporine and tacrolimus), or emergency colectomy.
6. Treatment Targets and Disease Monitoring
6.1 Patient-reported outcomes are short-term treatment targets associated with patient well-being.
6.2 Biomarkers
6.2.1 FC is a sensitive, noninvasive biomarker for correlating to endoscopic indices, assessing disease activity, and detecting relapse in patients with UC.
6.2.2 CRP and ESR can serve as adjunctive markers for assessing treatment response in UC.

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https://doi.org/10.5217/ir.2023.00050 • Intest Res 2024;22(3):213-249

Table 5. Continued

6.3 IUS can be used to monitor disease activity and treatment response.
6.4 Endoscopy
6.4.1 Endoscopic remission in UC is associated with improved long-term clinical outcomes.
6.4.2 Endoscopic reassessment should be considered in cases of relapse, refractoriness, the development of new symptoms, or when surgical intervention or changing therapy is indicated.
6.5 Achieving histological remission is valuable in predicting long-term remission and preventing cancer development. The Nancy index is a simplified histological score for monitoring histologic activity.
7. Surgery
7.1 Life-threatening conditions (e.g., bowel perforation, massive bleeding, toxic megacolon, and fulminant colitis refractory to medical treatment) are indications for emergent surgery. Persistent symptoms or intolerable side effects related to medical treatment, high-grade dysplasia, or carcinoma are indications for elective surgery.
7.2 Preoperative conditions, including nutrition status, immunosuppressant use, and overall performance, should be optimized before surgery. Weaning of steroid as possible should be considered for patients who are under high-dose steroid therapy.
7.3 The 3-stage procedure is probably safer for high-risk patients, such as those with severe colitis; on preoperative biologics, immunomodulators, or high-dose steroids; with malnourishment; or with anemia. The timing of pouch creation should be tailored to each patient based on their history and presentation, as well as the surgeon's expertise.
7.4 Total colectomy with ileorectal anastomosis could be an option in selected patients with UC and relative rectal sparing. Regular surveillance of the rectum is mandatory due to the potential risk of cancer.
8. Special Groups Consideration
8.1 Maintaining remission is associated with better pregnancy outcomes. A multidisciplinary team care with preconception consultation is suggested.
8.2 Most conventional and biological agents could be maintained during pregnancy, except small molecules.
8.3 For pediatric patients, long-term corticosteroid should be avoided.
8.4 For pediatric patients with moderate to severe UC who failed conventional agents, infliximab and adalimumab could be considered.
8.5 Since polypharmacy and comorbidities are common in elder patients, concomitant infection and drug interactions should be taken into consideration.
8.6 Adequate disease control is as important in elder patients as the younger patients to decrease the UC related complications.
9. CRC Surveillance
9.1 Since patients with UC are at increased risk of developing CRC, disease control and regular surveillance are essential.
9.2 Colonoscopic surveillance for dysplasia should be offered to all patients 8 years after the onset of UC. Those with concurrent PSC should receive a colonoscopy immediately, and annual surveillance is recommended.
9.3 The surveillance technique
9.3.1 High-definition colonoscopy with targeted biopsies is recommended for surveillance. Random biopsies could be performed in some special cases, such as in PSC, lead pipe colon, and previous dysplasia areas.
9.3.2 DCE is preferred over white-light standard colonoscopy. Virtual chromoendoscopy could be an alternative to DCE to detect dysplasia while using a high-definition colonoscope.
9.4 When dysplasia in UC is endoscopically resectable, endoscopic resection could be considered. However, subsequent surveillance at adequate interval should be performed.
9.5 When dysplasia in UC is high-grade, multifocal or endoscopically unresectable, surgical consultation is recommended.

UC, ulcerative colitis; EIMs, extraintestinal manifestations; ASUC, acute severe ulcerative colitis; IUS, intestinal ultrasound; HBsAg, hepatitis B surface antigen; anti-HBs, hepatitis B surface antibody; anti-HBc, hepatitis B core antibody; HBV, hepatitis B virus; TB, tuberculosis; IGRA, interferon-gamma release; TST, tuberculin skin test; LTB, latent tuberculosis; EN, enteral nutrition; PN, parenteral nutrition; 5-ASA, 5-aminosalicylic acid; MMX, multi-matrix; IV, intravenous; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; CRC, colorectal cancer; PSC, primary sclerosing cholangitis; DCE, dye spray chromoendoscopy.

rithms (overall UC treatment and ASUC) serve as a concise and practical tool designed to support clinicians in Taiwan in their clinical decision-making (Figs. 1 and 2). Ensuring an accurate UC diagnosis involves comprehensively excluding potential differential diagnoses and carefully evaluating disease severity based on clinical, endoscopic, and histological findings. The treatment strategy is determined based on disease severity, typically involving the use of 5-ASA, corticosteroids,

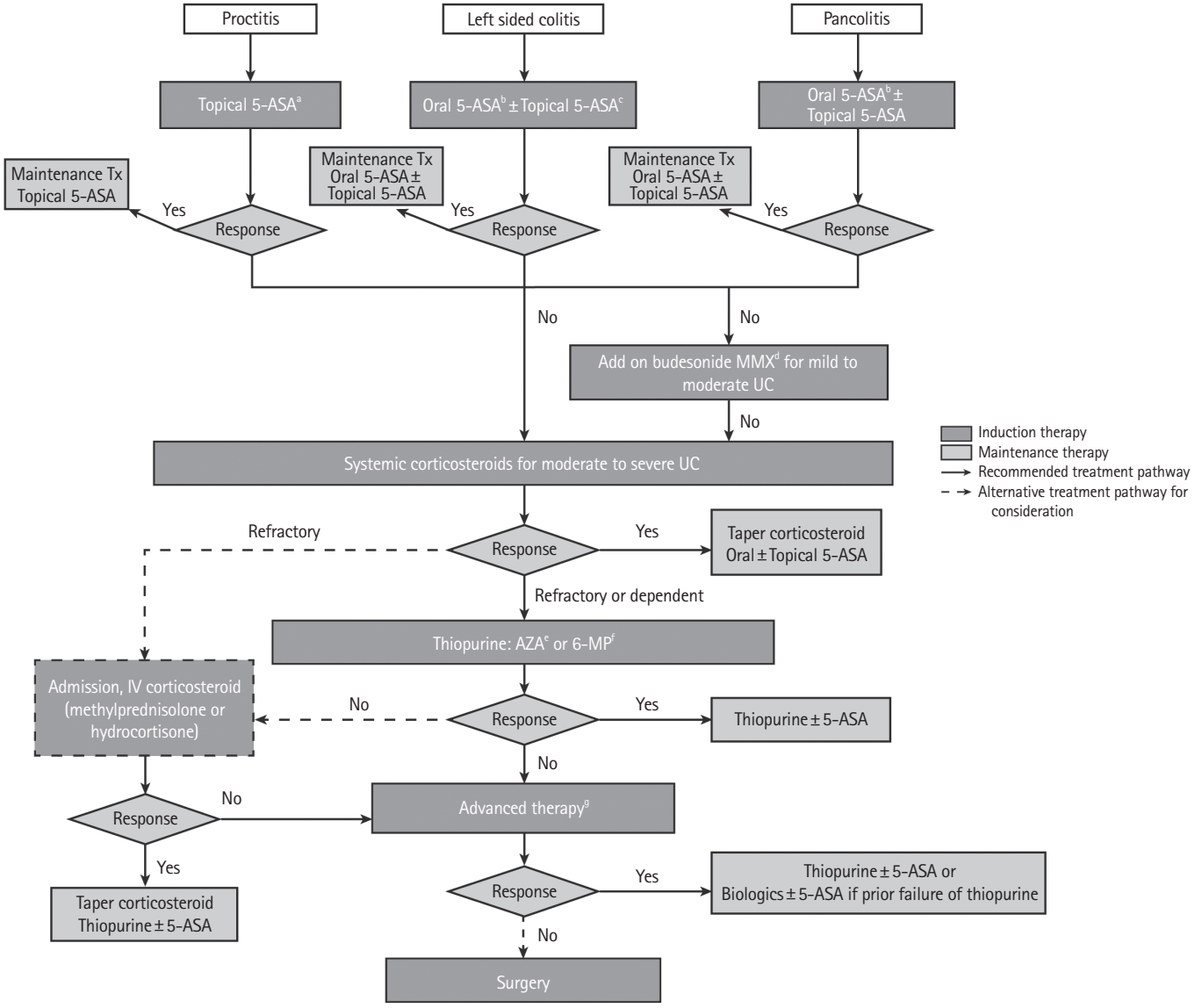

Fig. 1. Recommended algorithm for the treatment of UC. [a]1 g/day. [b]≥ 2 g/day. [c]≥ 1 g/day. [d]9 mg/day. [e]1.0–2.5 mg/kg/day. [f]0.45–1.5 mg/kg/day. [g]Anti-tumor necrosis factor (infliximab, adalimumab; golimumab), vedolizumab, ustekinumab, JAK inhibitors (tofacitinib, upadacitinib) or ozanimod. 5-ASA, 5-aminosalicylic acid; Tx, treatment; MMX, multi-matrix; UC, ulcerative colitis; AZA, azathioprine; 6-MP, 6-mercaptopurine; IV, intravenous.

immunomodulators, and advanced therapy (biologics and small molecules). The presented recommendations, grounded in current evidence, may undergo future revisions as additional data on existing and novel therapeutics for UC become available.

ADDITIONAL INFORMATION

Funding Source

The authors received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest

Wong JM and Wei SC are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

Data Availability Statement

Not applicable.

https://doi.org/10.5217/ir.2023.00050 • Intest Res 2024;22(3):213-249

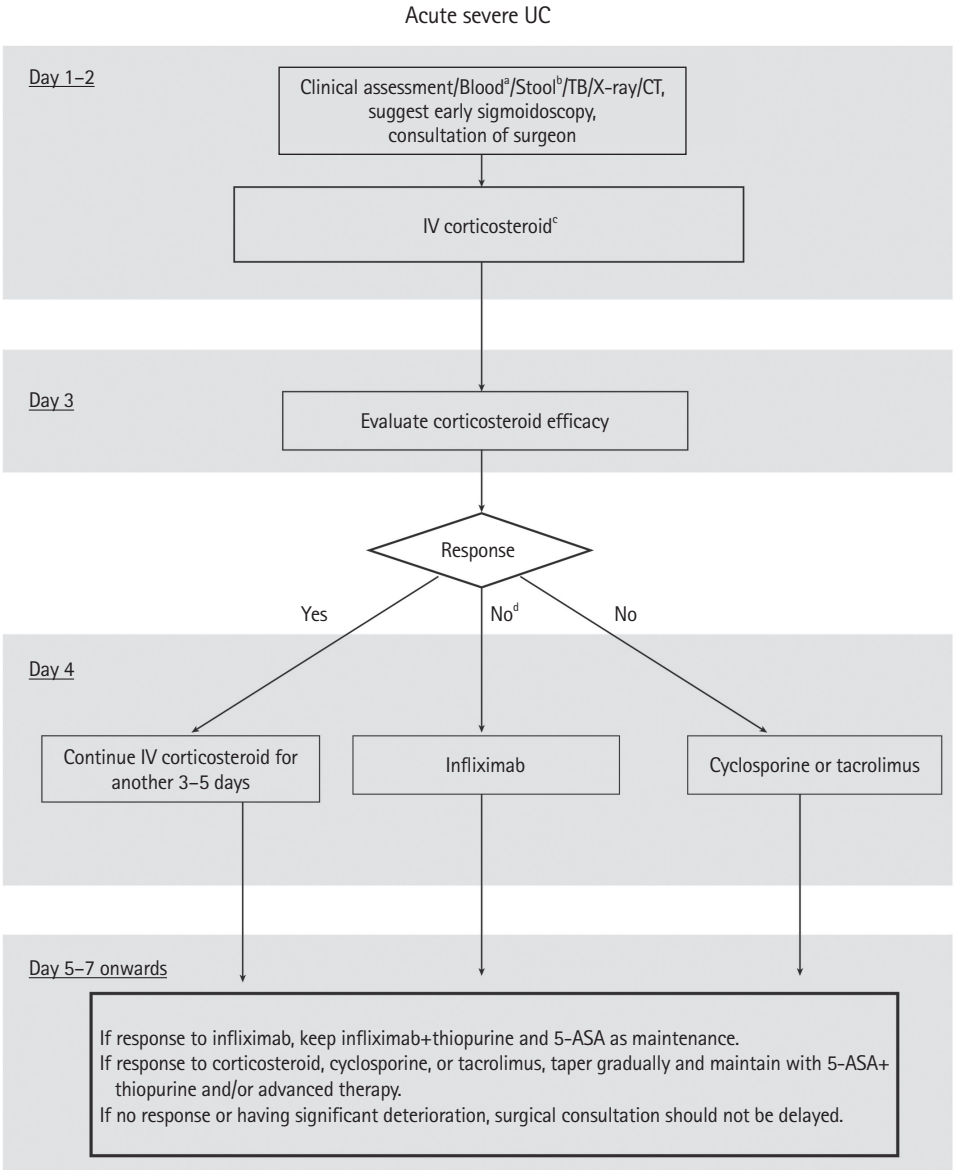

Fig. 2. Recommended algorithm for the treatment of acute severe ulcerative colitis (UC). [a]Complete blood count, C-reactive protein, electrolytes, liver enzymes, hepatitis B virus, hepatitis C virus, etc; [b]Stool culture, Clostridium difficile toxin, viruses; [c]Methylprodcisionle 1 mg/kg/day or 60 mg/day, maximally, or hydrocortisone 100 mg × 4 times daily, maximally; [d]Treatment failure, C-reactive protein > 4.5 mg/dL & blood stool 3–8 times/day or bloody stool > 8 times/day. TB, tuberculosis; CT, computed tomography; IV, intravenous; 5-ASA, 5-aminosalicylic acid.

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