A Questionnaire-Based Survey on the Diagnosis and Management of Inflammatory Bowel Disease in East Asian Countries in 2012

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Key Words

Inflammatory bowel disease · East Asian countries · Questionnaire · Ulcerative colitis · Crohn's disease · *Cytomegalovirus*

Abstract

Background and Aim: The prevalence and incidence of inflammatory bowel disease (IBD) are lower in East Asia than in Western countries; however, marked increases have recently been reported. The clinical diagnosis and medical management of IBD in East Asia differ from those in Western countries. A questionnaire-based survey was performed to gather physicians' current opinions on IBD in different East Asian countries. **Methods:** Representative International

Gastrointestinal Consensus Symposium (IGICS) committee members provided a questionnaire to physicians in each East Asian country studied. The questionnaire mainly focused on the diagnosis and management of IBD. **Results:** There were 19 respondents from Japan, 10 from South Korea, 9 from the Philippines, 6 from China and 4 from Indonesia. Colonoscopy (100%) and histopathology (63%) were commonly used for the diagnosis in ulcerative colitis (UC). Conventional small bowel enteroclysis was still the most common diagnostic tool for assessing small bowel lesions in Crohn's disease (CD) in East Asia. The percentage of physicians who investigated the reactivation of *Cytomegalovirus* in severe or refractory patients with UC ranged from 0% in the Philippines and Indonesia to 100% in Japan and Korea. Most physicians in Korea, the Philippines, China and Indone-

sia chose thiopurines or anti-TNF therapy as the second-line treatment in severe refractory UC, whereas Japanese physicians preferred to use tacrolimus or leukocyte apheresis. Physicians in the Philippines and Indonesia preferred to use oral 5-aminosalicylic acid for newly diagnosed severe ileocecal CD. In contrast, Korean physicians chose oral steroids and most physicians in China and Japan preferred to use anti-TNF. Nutritional therapy to induce or maintain remission in patients with CD was commonly used in Indonesia, Japan and China. Targeted biopsies by conventional colonoscopy were the most preferred strategy for cancer surveillance in long-standing UC over random biopsies in this region. **Conclusions:** The present survey found that current diagnostic approaches and clinical management of IBD vary within East Asian countries.

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Introduction

The incidence and prevalence of inflammatory bowel disease (IBD) are lower in East Asia than in Europe and the USA; however, marked increases have recently been reported [1]. When physicians in East Asia diagnose and treat IBD, they basically refer to the guidelines used in Western countries because there are many patients with IBD in those countries. However, the treatment and diagnosis of IBD in East Asia differ from those in Western countries, and have been attributed to differences in the environment, genetic background, available diagnostic and treatment methods, and health insurance system. East Asian physicians have to exclude intestinal tuberculosis and intestinal Behcet disease to confirm a diagnosis of IBD, whereas the incidences of these diseases are low in the West. In addition, several therapeutic drugs used for IBD in the West are not available in some East Asian countries. On the other hand, there are treatment options that are characteristic of this region and not generally used in the West, such as leukocyte apheresis in Japan and medical herbs in China. Considering these differences, the IBD management consensus was formulated in the Asia-Pacific region in 2005 and 2010 [2, 3]. In addition, there are original diagnostic criteria, guidelines and consensus in China, Korea and Japan, and various differences in the diagnosis and treatment of IBD among East Asian countries [4–9].

A marked change has recently occurred in the diagnostic and treatment methods for IBD. Video capsule endoscopy and balloon enteroscopy have rapidly spread as new imaging diagnostic methods for lesions of the small intestine of Crohn's disease (CD), and MR enterography

or enteroclysis is now recommended by guidelines in the West [10]. Internal medicinal treatment for patients with intractable IBD has rapidly advanced, and treatment options have increased. For example, in Japan, tacrolimus, infliximab and adalimumab were approved for the treatment of intractable ulcerative colitis (UC) in 2009, 2010 and 2013, respectively. On the other hand, new problems to be solved appeared with changes in the diagnostic and treatment methods for IBD. The following new topics are now being discussed worldwide: (1) indications and differential use of novel treatment methods, (2) the importance of mucosal healing, (3) diagnosis and treatment of opportunistic infections, particularly *Cytomegalovirus* (CMV) and *Clostridium difficile* infections, (4) treatment of patients for whom the effect of anti-TNF therapy becomes insufficient (loss of response), (5) the necessity of anti-TNF/immunomodulator combination therapy, (6) indication of anti-TNF for the postoperative recurrence-preventive treatment of CD and (7) the optimum diagnostic method and management for colitis-associated colorectal cancer or dysplasia [10–16]. No consensus has been reached for many of these topics, even in the West.

A questionnaire-based survey was performed to investigate the state of diagnostic and treatment methods for IBD in East Asia in 2007 [9]. Five years later, the diagnostic and treatment methods for IBD have markedly changed, as described above, and the actual state of the selection of new diagnostic and treatment methods for IBD in East Asia is currently unclear. Moreover, the opinions of East Asian physicians on new topics concerning the diagnosis and treatment of IBD have not been determined. In this study, we performed a questionnaire-based survey to collect the opinions of East Asian physicians regarding the current diagnostic and treatment methods for IBD.

Subjects and Methods

This is the 6th questionnaire-based survey conducted by the International Gastrointestinal Consensus Symposium (IGICS), which is the international section of the Japanese Gastroenterological Association. Gastroenterologists and physicians involved in the clinical treatment of IBD at major institutions in China, South Korea, Japan, the Philippines and Indonesia participated in this survey. All participants work in an urban environment.

Representative IGICS committee members provided a questionnaire to the selected physicians in each country, starting in July 2012. Responses were collected by electronic mail until the end of December 2012. The questionnaire contained 32 questions focused on the following items: (1) diagnosis of IBD, (2) infections in IBD, (3) management of IBD and (4) cancer surveillance in IBD. Details of the questionnaire are shown in the Appendix.

Fig. 1. Annual numbers of UC and CD patients treated at institutions in each country. Data are presented as the mean, maximum and minimum values.

Fig. 2. Differential diagnosis of IBD in East Asia. **a** Main diseases to be differentiated from UC. **b** Main diseases to be differentiated from CD.

Results

Characteristics of Respondents

A total of 48 physicians participated in the survey; 19, 10, 9, 6 and 4 responded from Japan, Korea, the Philippines, China and Indonesia, respectively. Of these respondents, 58% were IBD experts.

The median annual numbers of UC and CD patients treated at the institutions to which the respondents be-

longed in each country are shown in figure 1. Both numbers were the highest in Korea. The number of patients with UC was higher than that of patients with CD in all institutions in all East Asian countries that were surveyed. The mean annual number of IBD patients at the institutions to which IBD experts belong was 525.3 ± 778.4 , while that at institutions without an expert was 84.2 ± 103.8 .

Fig. 3. Examinations for the diagnosis and assessment of disease activity in IBD. **a** Examinations for the diagnosis and assessment of disease activity in UC (multiple answers allowed). **b** Examinations for the diagnosis and assessment of disease activity in CD

(multiple answers allowed). **c** Percentage of physicians who considered upper gastrointestinal endoscopy to be important in the diagnosis of CD in each country. **d** First-line tool used for assessing small bowel lesions in CD.

Diagnosis of IBD

Differential Diagnosis of IBD

Bacterial gastroenteritis was included in diseases to be differentiated from UC by 58% of the respondents, followed by CD, intestinal tuberculosis and amoebic colitis (fig. 2a). Intestinal tuberculosis was included in diseases to be differentiated from CD by 60% of the respondents, followed by UC, bacterial gastroenteritis and intestinal Behcet disease (fig. 2b).

Examinations for Diagnosis and Assessment of Disease Activity in IBD

Regarding examinations to diagnose UC and evaluate its disease activity, 100% of the respondents stated that they perform colonoscopy, followed by histopathology (63%; fig. 3a). Fecal calprotectin is available in a limited number of institutions in East Asia, and 10% of the respondents use it.

CD is currently diagnosed using ileocolonoscopy by 90% of the physicians, followed by histopathology (60%), upper gastrointestinal endoscopy (50%) and various imaging diagnostic methods (13–17%) to evaluate lesions of the small intestine (fig. 3b). Opinions varied among the East Asian countries regarding the importance of upper gastrointestinal endoscopy to diagnose CD (fig. 3c). Upper gastrointestinal endoscopy was considered important to diagnose CD by 75% or more of the physicians in Japan, the Philippines and Indonesia, and by approximately 35% of the physicians in China and Korea. The most useful endoscopic finding to diagnose CD was longitudinal ulcer (52%), followed by a cobblestone appearance (50%), discontinuous involvement (42%), multiple aphthae (17%) and stricture (10%). The most common first-line test to evaluate lesions of the small intestine of CD was conventional small bowel enteroclysis or small bowel follow-through (46%; fig. 3d). In contrast, the frequency of using MR enterography or enteroclysis was only 2%. Moreover, 14% of the respondents answered that video capsule endoscopy was the first-line imaging examination of the small intestine.

Regarding questions concerning the use of clinical disease activity indices in routine medical practice, 60 and 58% of the respondents used the indices for UC and CD, respectively. The most commonly used clinical activity index of UC was the Modified Mayo score (38%), followed by Truelove and Witts' index (28%), Sutherland index (25%), and Lichtiger index (17%). Regarding CD, 89% of the respondents used the CD activity index. Ninety percent of the respondents agreed that the combination of improvements in clinical symptoms and endo-

scopic mucosal healing was the best means of judging IBD remission.

Infections in IBD

The response to whether the reactivation of CMV is examined in severe or refractory UC patients varied markedly among the countries. In Japan and Korea, 100% of physicians examine the reactivation of CMV, while only 50 and 0% of physicians do so in China and the Philippines, respectively (fig. 4a). The diagnostic method of CMV infection and reactivation also varied among the countries. In Japan, CMV antigenemia was most commonly examined, while histopathology and CMV serum antibodies were commonly examined in Korea and China, respectively (fig. 4b). In addition, 78% of East Asian physicians stated that antiviral treatment improved the outcome of CMV-positive UC patients. The rate of physicians who investigate *C. difficile* infection in severe or refractory UC patients ranged from 44% in the Philippines to 90% in Korea (fig. 4c).

Management of IBD

Available Drugs and Treatment Methods

Table 1 shows a list of therapeutic drugs and treatment methods for IBD available at institutions in the participating countries at the time of the survey. Limited oral and topical 5-aminosalicylic acid (5-ASA) were available in Japan, the Philippines and Indonesia. Only in Japan could budesonide not be used. Tacrolimus was used in Japan, Korea and the Philippines. Apheresis was used in some institutions in Japan, the Philippines and China.

Management of UC

The treatment methods employed for the initial onset of mild-moderate distal-type UC are shown in figure 5a. Fifty percent of the respondents selected oral 5-ASA, 42% selected a combination of topical and oral 5-ASA, and 8% selected topical 5-ASA. A combination of topical and oral 5-ASA was the most preferred in Korea.

The treatment methods employed for the initial onset of mild-moderate extensive colitis are shown in figure 5b. A combination of topical and oral 5-ASA was the most preferred, followed by oral steroids. Various types of topical 5-ASA are available in Korea and China, and physicians in these countries were more likely to select a combination of topical and oral 5-ASA over oral steroids.

The treatment methods employed for the initial onset of severe extensive colitis are shown in figure 5c. Sixty-four percent of the respondents selected intravenous steroids, followed by oral 5-ASA (44%) and oral steroids

Fig. 4. Infections in IBD. **a** Percentage of physicians who investigate the reactivation of CMV in severe or refractory patients with UC. **b** Diagnostic tools for the identification of CMV infection (multiple answers allowed). **c** Percentage of physicians who perform a stool test for *C. difficile* in severe or refractory patients with UC.

Fig. 5. Management of UC. **a** Treatment for newly diagnosed mild-moderate distal colitis (multiple answers allowed). **b** Treatment for newly diagnosed mild-moderate extensive colitis (multiple answers allowed). **c** Treatment for newly diagnosed severe extensive colitis (multiple answers allowed). **d** Second-line treatment for severe extensive colitis (multiple answers allowed).

(26%). Several Japanese physicians selected leukocyte apheresis or granulocyte and monocyte adsorptive apheresis over steroids.

To treat severe extensive colitis cases not responding to the first-line treatment, many physicians in Korea, the Philippines, China and Indonesia selected thiopurine or anti-TNF therapy as the second-line treatment (fig. 5d).

In contrast, many Japanese physicians preferred tacrolimus or leukocyte apheresis to thiopurine and anti-TNF therapy.

Management of CD

The treatment methods employed for the initial onset of mild-moderate ileocecal CD are shown in figure 6a.

Table 1. Therapeutic drugs and treatment methods for IBD available at the institutions that participated in the survey

	Japan	South Korea	The Philip-pines	China	Indo-nesia
<i>Oral 5-ASA</i>					
SASP	○	○	○	○	○
Pentasa	○	○	○	○	
Asacol	○	○		○	
Salofalk		○	○	○	○
Balsalazide		○		○	
Olsalazine		○		○	
<i>Topical 5-ASA</i>					
SASP sp	○	○	○	○	
Pentasa sp		○	○	○	
Pentasa enema	○	○	○	○	
Pentasa foam		○		○	
Salofalk sp		○	○		○
<i>Corticosteroids</i>					
Prednisolone	○	○	○	○	○
Budesonide		○	○	○	○
<i>Immunomodulators</i>					
AZA/6-MP	○	○	○	○	○
Cyclosporine	○	○	○	○	
Tacrolimus	○	○	○		
<i>Biologics</i>					
Remicade	○	○	○	○	○
Humira	○	○		○	
<i>Apheresis</i>					
GMA/LCAP	○		○	○	

SASP = Salazosulfapyridine; sp = suppository; AZA = azathioprine; 6-MP = 6-mercaptopurine; GMA = granulocyte and monocyte adsorptive apheresis; LCAP = leukocyte apheresis.

Excluding Indonesia, in which oral steroids including budesonide are preferred, oral 5-ASA was the most preferred treatment in East Asian countries.

Treatment for the initial onset of severe ileocecal CD markedly varied among the countries (fig. 6b). The number of physicians that selected oral 5-ASA was the largest in the Philippines and Indonesia. In contrast, many Korean physicians selected oral steroids, and anti-TNF was most frequently selected by Chinese and Japanese physicians.

Enteral nutritional therapy to remit and maintain the remission of CD was commonly performed in Indonesia, Japan and China, and was less frequently performed in the Philippines and Korea (fig. 6c).

Figure 6d shows the treatment policies selected for patients for whom the effect of anti-TNF therapy became insufficient. Dose escalation was selected by 40% of the East Asian physicians, followed by a switch to other biologics (25%), reduction in the interval between injections (23%), and consideration of surgical treatment (21%).

Physicians' opinions regarding the frequency of combining an immunomodulator with anti-TNF therapy were divided among the countries (fig. 6d). All Korean physicians always or often use a concomitant immunomodulator with anti-TNF therapy, whereas fewer physicians in other countries consider this combination essential. Opinions on the duration of anti-TNF/immunomodulator combination therapy also varied (fig. 6e), and the rates of the duration of combination therapy limited to within 6 months and 2 years or longer were equivalent (24%). Regarding the intensification of treatment for CD patients in whom the clinical condition was in remission with mucosal healing not yet being achieved endoscopically, 56 and 23% of the respondents answered that intensification was necessary and unnecessary, respectively, and 21% answered that they did not know.

Figure 6f shows the postoperative prophylactic treatments preferred for postoperative CD patients at a high risk of recurrence. In the Philippines, China and Indonesia, 5-ASA was most commonly used as the postoperative recurrence-preventive treatment. In contrast, Korean and Japanese physicians preferred to use thiopurines and anti-TNF to avoid the postoperative recurrence of CD, respectively.

Cancer Surveillance and Management of Neoplastic Lesions in IBD

Cancer Surveillance in IBD

Figure 7a shows the cancer surveillance methods used for patients with chronic UC. Targeted biopsies by conventional colonoscopy were preferred to random biopsies (4 every 10 cm) in the East Asian countries, excluding the Philippines. Although targeted biopsies by pan-colonic chromoendoscopy are recommended by guidelines in the West, this was not commonly used in East Asia.

Figure 7b shows the opinions of the physicians on the usefulness of new endoscopic imaging techniques (narrow-band imaging, autofluorescence imaging and magnifying colonoscopy with pit pattern analysis) to diagnose neoplastic lesions complicating UC. Since only a limited number of institutions use these modalities, many physicians said that they did not know, while other physicians considered these modalities useful.

Fig. 6. Management of CD. **a** Preferred treatment for newly diagnosed mild-moderate ileocecal CD (multiple answers allowed). **b** Preferred treatment for newly diagnosed severe ileocecal CD (multiple answers allowed). **c** Percentage of physicians who use nutritional therapy for the induction or maintenance of remission in patients with CD.

Fig. 6. Management of CD. **d** Preferred strategy for patients with the initial loss of a response to anti-TNF therapy. **e** Percentage of physicians who concomitantly use an immunomodulator with anti-TNF therapy for CD patients. **f** Duration of the combination of an immunomodulator with anti-TNF therapy in CD patients.

Fig. 6. Management of CD. **g** Postoperative prophylactic treatment for CD patients at a high risk of recurrence (multiple answers allowed).

Fig. 7. Cancer surveillance. **a** Strategy for surveillance colonoscopy in UC. **b** Opinions of the physicians on whether or not new endoscopic imaging techniques are useful for the detection of neoplasia in UC.

Regarding the necessity of cancer surveillance colonoscopy for patients with extensive Crohn's colitis, 79, 13 and 8% of the respondents answered 'necessary', 'unnecessary', and 'I do not know', respectively.

Management of Neoplastic Lesions in IBD

In response to whether they recommend proctocolectomy to patients in whom flat low-grade dysplasia was observed on surveillance colonoscopy, 19, 74 and 7% of the respondents answered 'yes', 'no', and 'I do not know', respectively. Regarding the treatment of adenoma-like masses without flat dysplasia in the surrounding mucosa, 85% of the respondents answered that endoscopic treatment is appropriate.

Discussion

This survey was performed to investigate the opinions of physicians on the current state of diagnosis and treatment of IBD in East Asia. The number of IBD patients per institution was the largest in Korea, followed by Japan and China. This survey investigated the approximate annual number of patients treated in each institution, and does not accurately reflect the incidence and prevalence of IBD in each country. However, marked increases have been reported in the incidence and prevalence of IBD over the last 10–20 years in Japan, Korea and China, suggesting that the results of this survey are consistent with the actual situation [17–20]. Consistent with previous studies, there are generally more UC than CD patients in the East Asian countries surveyed [1]. The results of this survey confirmed that a large number of patients are treated at institutions to which experts belong because specialized knowledge is needed to treat IBD patients.

There is no gold standard for the diagnosis of IBD. It is diagnosed comprehensively based on the medical history of the patients, a clinical evaluation, typical endoscopic, histological and radiological findings, and the exclusion of similar diseases. To accurately diagnose IBD in East Asian countries, epidemic infectious diseases must be excluded. The tuberculosis infection rate, in particular, is high in Asia, and was listed in the top diseases to be differentiated from IBD.

Regarding the test methods used to diagnose and evaluate disease activity, colonoscopy (preferably with ileoscopy) and histopathology were preferred for both UC and CD. Variations were noted in opinions on the usefulness of upper gastrointestinal endoscopy to diagnose CD

among the East Asian countries. A high frequency of upper gastrointestinal tract involvement in CD patients has been reported [21]. Focal gastritis consistent with CD, as confirmed by gastric biopsies, may be useful to definitely diagnose CD. In Japan, characteristic gastric and duodenal lesions are secondary features of the diagnostic criteria, and physicians are more likely to actively perform upper gastrointestinal endoscopy. However, this may only be performed in CD patients with upper gastrointestinal symptoms in countries in which fewer physicians consider upper gastrointestinal endoscopy important.

Conventional small bowel enteroclysis is still the common first-line test used to evaluate lesions of the small intestine in CD patients in East Asia. MR and CT enterography or enteroclysis are recommended as the current standard in guidelines in the West, but these were used less frequently [10]. This finding is similar to that in the survey performed in 2007, suggesting that diagnosing lesions of the small intestine using MR and CT has not progressed in East Asia [9]. Since radiation exposure and the low sensitivity associated with barium studies are problematic, the more frequent use of MR enterography or enteroclysis is desired in this region. In our survey, 14% of the respondents answered that the first-line imaging examination of the small intestine is video capsule endoscopy. Since video capsule endoscopy is superior in diagnosing superficial mucosal lesions by excluding marked stenosis using a patency capsule, it may be more frequently used as the first-line imaging examination of the small intestine.

The classification of IBD based on disease activity and severity is important because it influences the decision on a treatment policy. More than half of the respondents use a clinical disease activity index, which was attributed to 58% of the respondents being IBD experts and many of them using these indices. These indices may be less frequently used in actual routine medical practice.

The involvement of CMV colitis in poor outcomes and a higher colectomy rate in IBD has been reported [22]. Despite the CMV seroprevalence being high in East Asia [23, 24], the rate of physicians who investigate CMV reactivation in patients with severe or refractory UC varied among these countries from 0 to 100%, and this may have been due to the current situation in which no conclusion has been reached regarding whether CMV infection in IBD patients is nonpathogenic colonization or a pathogenic disease requiring antiviral treatment [3, 25, 26]. Moreover, various diagnostic methods are used in these countries because no gold standard diagnostic method for CMV infection and disease has been sufficiently established.

Guidelines in the West recommend screening of *C. difficile* in each recurrence in IBD patients with lesions of the large intestine [13]. A retrospective observational study performed at a US referral center reported a marked increase in *C. difficile* infection in IBD patients [27]; however, whether it is similarly increasing in East Asia remains unclear. In our survey, the rate of physicians who investigate *C. difficile* infection in patients with severe or refractory UC varied among the countries, similar to that for CMV.

Various differences were also noted regarding the management of IBD among the East Asian countries. These differences may have been due various factors, such as the presence or absence of local guidelines and treatment guidance, differences in approved drugs and treatment, and economic factors. Topical/oral 5-ASA combination therapy is well known to be more effective at inducing the remission of active UC than individual treatments. In Korea and China, in which many types of topical 5-ASA are available, a combination of topical and oral 5-ASA was preferred to oral 5-ASA or oral steroid alone for treating the onset of initial mild-moderate UC.

Several Japanese physicians selected leukocyte apheresis as the first- or second-line treatment for severe extensive colitis. Since leukocyte apheresis, a treatment method developed in Japan, can be expected to show an effect equivalent to that of steroids for early moderate-severe UC, while exhibiting less adverse effects, it is recommended by Japanese local guidelines [8, 28]. However, its spread in other East Asian countries is insufficient and this may be due to the lack of high-quality evidence and poor cost-effectiveness. Tacrolimus and leukocyte apheresis were preferred as the second-line treatment for first-line treatment-resistant severe extensive colitis in Japan, whereas thiopurine and anti-TNF therapy were preferred in the other countries. No consensus has been reached with regard to optimum second-line treatment for intractable UC, and treatment may be selected based on the patient's age, consultation status (in- or outpatient), previous treatment, clinical background such as disease activity, available treatment methods and experience of the individual physicians.

Treatment for the initial onset of severe ileocecal CD varied among the countries. Many Chinese and Japanese physicians selected top-down therapy using anti-TNF antibodies, while physicians in the other countries were more likely to select oral steroids (step-up therapy). Japanese physicians actively perform anti-TNF therapy for postoperative CD patients with a high risk of recurrence.

Various factors have been considered for the difference observed in the use of anti-TNF, including insufficient evidence, an increase in the risk of opportunistic infections, high cost and differences in the health insurance system among the countries. In Japan, physicians do not have to limit the use of anti-TNF in consideration of the economic factors of patients because many IBD patients are supported by the public expenditure system. Therefore, it cannot be ruled out that anti-TNF is used more than necessary for IBD patients in Japan. An investigation on the cost-effectiveness of anti-TNF therapy and its appropriate use for IBD patients in Japan is needed.

The benefits of a combination with immunomodulators, such as anti-TNF with azathioprine, are currently being discussed [14]. Concomitant immunomodulatory therapy with anti-TNF for CD patients is strongly recommended in Korea, but is not actively performed in the other countries, and opinions remain divided. In the 1-year SONIC study, the combination of infliximab with azathioprine was more effective than infliximab alone for CD patients who were naive to both treatments [29]. However, combination therapy may induce hepatosplenic T cell lymphoma, particularly in young male patients [30]. Moreover, azathioprine was found to induce adverse reactions, such as neutropenia, more frequently in Asians than in Caucasians [31], which may be why only a limited number of physicians perform combination therapy in this region.

To date, no placebo-controlled trial of nutritional therapy for CD patients has been conducted. However, nutritional therapy exhibited an equivalent or slightly superior effect to corticosteroids on the remission induction of active CD in randomized controlled studies [32]. Nutritional therapy was also found to be useful for remission maintenance [33]. In our survey, enteral nutritional therapy was commonly performed in Indonesia, Japan and China, but less frequently in the Philippines and Korea. This difference may be due to the lack of patient acceptability and convenience, and evidence for its efficacy, although nutritional therapy is a safe treatment.

Greater importance has recently been attached to evaluating mucosal healing in IBD. Most respondents answered that it is most favorable to judge the remission of IBD based on the combination of improvements in clinical symptoms and endoscopic mucosal healing. The intensification of treatment of CD patients who achieved clinical remission without endoscopic mucosal healing is not recommended currently in Western guidelines [34]; however, 56% of the respondents considered it necessary.

The risk of colorectal cancer is well known to be higher in patients with long-term morbidity of IBD than in the general population. In Japan and Korea, the incidence of colorectal cancer complicating UC has been increasing [35, 36]. Surveillance colonoscopy is useful for the early discovery of colorectal cancer and is involved in improving the prognosis. The most preferred cancer surveillance method for patients with chronic UC in East Asian countries was targeted biopsies by conventional colonoscopy. However, evidence for colorectal cancer surveillance in targeted biopsies by conventional colonoscopy is currently insufficient, and is not recommended in guidelines in the West [13]. The reason for performing targeted biopsies by conventional colonoscopy in East Asia in spite of these conditions may be the presence of various problems associated with random biopsies, such as efficiency, burden on patients and endoscopists, and cost-effectiveness.

Proctocolectomy is commonly recommended for UC patients in whom dysplasia is detected on surveillance colonoscopy and histological evaluation. However, the carcinogenic risk of flat low-grade dysplasia was found to vary among studies, and its management is currently being discussed [13]. In our survey, only 19% of the physicians recommended proctocolectomy to UC patients with flat low-grade dysplasia.

Dysplasia-associated lesions or masses in UC are a heterogeneous group of tumors, and the carcinogenic risk is not equivalent among various subtypes [13, 37]. Adenoma-like masses are well-circumscribed, sessile or pedunculated neoplastic lesions without flat dysplasia similar to sporadic adenoma. Our survey clarified that most of the East Asian physicians surveyed considered adenoma-like masses to be indications of endoscopic resection.

In conclusion, the results of the survey clarified commonalities in the diagnostic approach and clinical management of IBD in East Asia, but also many differences.

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Appendix

The questionnaire used in the present survey.

Q1	How many UC/CD patients per annum do you have in your institution?
Q2	What are the major diseases in the differential diagnosis of UC/CD in your country?
Q3	What are the essential examinations used to diagnose and assess disease activity in UC/CD?
Q4	Do you think that upper gastrointestinal endoscopy is important for the diagnosis of CD?
Q5	What are the useful endoscopic features for diagnosing CD?
Q6	What is the first-line tool used to assess small bowel inflammatory lesions in CD?
Q7	Do you use the clinical disease activity indices for UC/CD in daily routine clinical practice?
Q8	If you answered 'yes' to Q7, what kind of index do you use?
Q9	Do you think that the best way of defining remission should be a combination of the clinical resolution of symptoms and endoscopic mucosal healing?
Q10	Do you commonly investigate the reactivation of <i>Cytomegalovirus</i> in severe or refractory patients with UC?
Q11	If you answered 'yes' to Q10, what kind of methods do you use to detect <i>Cytomegalovirus</i> infection in UC patients?
Q12	Do you think that treatment with antivirals improves the outcomes of UC patients with <i>Cytomegalovirus</i> infection?
Q14	Do you commonly perform a stool test for <i>Clostridium difficile</i> in severe or refractory patients with UC?
Q15	Which of the treatments described below are available in your country?
5-ASA (oral); 5-ASA (topical); corticosteroid; immunomodulator; apheresis; biologics.
Q16	What is your first choice for the treatment of newly diagnosed mild-moderate distal colitis?
Q17	What is your first choice for the treatment of newly diagnosed mild-moderate extensive colitis?
Q18	What is your first choice for the treatment of newly diagnosed severe extensive colitis?
Q19	What is your second-line treatment for severe extensive colitis?
Q20	What is your first choice for the treatment of newly diagnosed mild-moderate ileocecal CD?
Q21	What is your first choice for the treatment of newly diagnosed severe ileocecal CD?
Q22	Do you use nutritional therapy for the induction or maintenance of remission in patients with CD?

- Q23 Which strategy do you commonly choose for patients with the initial loss of a response to anti-TNF therapy?
- Q24 Do you recommend the combined use of anti-TNF therapy and an immunomodulator for patients with active CD refractory to conventional therapy?
- Q25 If you answered 'always' or 'often' to Q24, how long do you commonly use combination immunosuppressive therapy?
- Q26 Do you think that the intensification of treatment is needed for patients whose clinical remission is not associated with mucosal healing?
- Q27 What kind of postoperative prophylactic treatment do you choose for CD patients with high risk of recurrence?

- Q28 Which of the below strategies for cancer surveillance colonoscopy do you perform in your institution? Random biopsies (4 every 10 cm) + targeted biopsies; random biopsies (each colon segment) + targeted biopsies; targeted biopsies by conventional colonoscopy; targeted biopsies by NBI colonoscopy; targeted biopsies by pan-colonic chromoendoscopy.
- Q29 Do you think that NBI/AFI/magnifying colonoscopy is useful for the detection of neoplasia in UC?
- Q30 Do you think that surveillance colonoscopy should be performed for patients with extensive Crohn's colitis?
- Q31 Do you agree that a patient with low-grade dysplasia in flat mucosa should be offered proctocolectomy?
- Q32 Do you agree that endoscopic treatment is suitable for raised adenoma-like mass in the absence of flat dysplasia?

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