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Knowledge, attitudes, and practices of endoscopy among gastroenterologists in diagnosis and management of inflammatory bowel disease in China: a multicenter cross-sectional study

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Abstract

Background The aim was to assess the knowledge, attitudes, and practices (KAPs) of endoscopy among gastroenterologists in the diagnosis and management of IBD in China.

Methods A multicenter cross-sectional KAP study was performed. The questionnaire was developed and improved using feedback and opinions from a team of experienced IBD specialist professors and then distributed and collected online. In addition, eight fellow gastroenterologists participated in an IBD endoscopy training program were asked to review endoscopic images, and the consistency of the endoscopic scores before and after training was calculated.

Results A total of 193 participants from 12 provincial-level administrative regions encompassing both the Northern and Southern parts of China completed the study questionnaire. The median age of the participants was 40 (36, 45) years, with the majority being female (70.5%). The median professional experience as gastroenterologists was 11 (7, 17) years, while the median experience as endoscopists was 8 (3, 15) years. The median knowledge score was 8 out of 10 points for single-choice questions; however, most gastroenterologists believed that some concepts in these endoscopic indices were vague, including those regarding deep ulcerations, ulcerated surfaces, affected surfaces and narrowing in open-answer questions. The UCEIS and SES-CD were considered most consistent with clinical activity score in the evaluation of UC and CD, respectively. IBD subspecialists and gastroenterologists who had previously received IBD endoscopy screening training were more likely to use endoscopic indices ($p<0.001$, $p=0.029$, respectively). The Rutgeerts score demonstrated the most significant improvement in consistency before and after training, from 0.407 (95% CI: 0.025–0.999) to 0.909 (95% CI: 0.530–1.000).

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Conclusions We propose the elucidation of ambiguous definitions in endoscopic indices, enhancement of training, and the application of innovative technology to enhance the application of endoscopic evaluation and endoscopic indices in clinical practice.

Keywords Inflammatory bowel disease, Endoscopic index, Intraobserver reliability, Training

Introduction

Digestive endoscopy plays a great role in the diagnosis and management of inflammatory bowel disease (IBD). Patients undergo multiple endoscopic evaluations during the course of the disease, including gastroscopy, enteroscopy and colonoscopy. Endoscopic assessment results are an important part of patients' disease activity assessments, and treatment strategies may be adjusted based on endoscopic evaluation results [1].

At present, many endoscopic indices have been introduced [2]. The Mayo endoscopic score (MES) and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) are well and commonly used in ulcerative colitis (UC) patients. In clinical trials, an MES of 0 or 1 is a widely accepted criterion for mucosal healing. However in further analysis, patients with MES 1 presented much higher relapse rate during 6 months of follow-up than patients with MES 0 [3]. A lower MES at baseline for patients receiving induction therapy was associated with higher odds of remission in long-term follow-up [4]. The UCEIS accurately reflects clinical outcomes and predicts prognosis in UC patients, and higher MES score corelates with higher recurrence rate [5]. The Crohn Disease Endoscopic Index of Severity (CDEIS), the Simple Endoscopic Score for CD (SES-CD) and Rutgeerts Postoperative Endoscopic Index have been introduced for disease activity assessment in Crohn's disease (CD) patients. A CDEIS score below 3 or 4 was defined as endoscopic remission in CD patients in many clinical trials [6, 7]. A change in the SES-CD was set as the primary end point in clinical trials of ustekinumab [8]. A Rutgeerts score≥i2 at 6 months was considered endoscopic recurrence in CD patients who underwent surgery [9]. It is widely acknowledged that endoscopic evaluation is an important criterion for the evaluation of and treatment strategy for IBD.

Although these endoscopic indices are widely used in clinical practice, many gastroenterologists find it challenging to master them. The criterias are objective; however, the interpretation varies from person to person, which may influence the accuracy and restrict the use of these indices. Therefore, the aim of our study was to assess the knowledge, attitudes, and practices (KAPs) of endoscopy among gastroenterologists in the diagnosis and management of IBD. We also expected to improve the cognition of gastroenterologists regarding these indices, put forward target knowledge for training, and provide criteria for more objective evaluations of clinical efficacy.

Methods

Study design and population

This study was composed of two parts: The first was a multicenter, cross-sectional KAP study. The study population were selected though a three steps sampling. Initially, a convenience sampling method was employed to select 12 out of the 34 provincial-level administrative regions in China. Subsequently, one hospital was randomly chosen from each province. Finally, all gastroenterologists working at the selected hospitals were invited to participate in the survey through cluster sampling. All participants were willing to provide informed consent.

The study questionnaire was developed in Chinese after reviewing published literature. After an initial draft of the questionnaire was designed, it was improved using feedback and opinions from a team of experienced IBD specialist professors. The final questionnaire consisted of 4 sections and 38 questions. The first section collected data on sociodemographic characteristics, including age, sex, professional title, work experience and self-reported training experience. The second section assessed respondents' knowledge of commonly used endoscopic indices for IBD, which included 10 single-choice questions in the first draft and was expanded to include four nouns with vague or difficult definitions to set open-answer questions after seeking the opinions of experienced IBD experts, who had more than 10 years of clinical experience in the field of IBD. For the 10 single-choice questions, knowledge score was calculated as the total number of correct responses. One point was assigned to each correct response and zero otherwise. The third section assessed respondents' attitudes toward endoscopic indices for IBD, and the fourth section assessed respondents' practices in IBD endoscopy assessment (Appendix 1). To eliminate bias, open answer choice was set in subjective questions.

The questionnaire was distributed and collected online between December 2022 and January 2023. We used Wenjuanxing Platform to distribute the questionnaire, which is a widely used online survey platform in China. Wenjuanxing Platform claims to have strict rules in accessing user data. All participants were anonymous in answering the questionnaire.

Eight fellow gastroenterologists participated in an IBD endoscopy training program at Peking Union Medical College Hospital in October 2022 and agreed to participate in this study.The training program included both theoretical lectures and clinical practice. Trainees were

required to observe or perform colonoscopies under guidance of experienced gastroenterologists in our hospital. And they received lectures using images or videos every week. Given the limited number of participants, we conducted a sample size calculation when selecting the images. According to "sample size formulas for estimating intraclass correlation coefficients with precision and assurance [10]", endoscopy images from 14 patients were chosen to evaluate accuracy and consistency of the endoscopic scores before and after training. Before training, the endoscopy images of 14 patients (including 7 UC patients, 5 CD patients and 2 postoperative CD patients) were shown. We had around 60 images for each patient, and participants were asked to independently review at least 8 pictures of different location of each patient to give MES and UCEIS score for UC patients, CDEIS and SES-CD for CD patients, and Rutgeerts score for postoperative CD patients. After training, all participants were asked to review and score the endoscopic images a second time. The correct scores were given by two senior IBD specialists. Participants did not know each other's answers or the correct answers.

Statistical analysis

Data were downloaded in Excel format from the Google server, verified for accuracy and consistency, and then imported to IBM's SPSS software version 24.0 (Armonk, NY, USA) for analysis. Continuous variables were reported as the means and standard deviations if the data followed a normal distribution, or the medians and interquartile ranges otherwise. Categorical variables were expressed as frequencies and proportions. The knowledge scores were calculated as continuous variables by summing the number of correct responses. One point was assigned to each correct response and zero points were assigned otherwise. Chi-square tests were performed to determine the association between the demographic characteristics and knowledge, attitudes, and practices of participants toward IBD endoscopy screening. Intraobserver agreement among the participants before and after training was determined using the intraclass correlation coefficient (ICC). The reliability according to the ICC was interpreted as poor (<0.5), moderate (0.5–0.75), good (0.75–0.90) and excellent (>0.90) [11]. The statistical significance for all tests was set at $p<0.05$.

Table 1 Sociodemographic characteristics of the study population

Characteristics	Frequency, *N* (%)
Gender	
Female	136 (70.5)
Male	57 (29.5)
Technical title	
Resident	16 (8.3)
Attending	75 (38.9)
Associate senior title or associate professor	70 (36.3)
Senior title or professor	32 (16.6)
Sub-specialty	
IBD sub-specialty	108 (56.0)
Non IBD sub-specialty	85 (44.0)
Previous training experience in IBD endoscopy screening	
Yes	103 (53.0)
No	90 (47.0)

Ethics approval and consent to participate

This study was approved by the Ethical Committee of Peking Union Medical College Hospital (PUMCH) (No. I-23ZM0023). Consent was obtained from each participant in the questionnaire and before training, and participation in the KAP study and endoscopy training was voluntary. The questionnaires were completely anonymous and did not include any data that could be used to identify the respondents.

Results

General characteristics of study participants

A total of 215 gastroenterologists were invited to participate online, however 193 of them completed the study questionnaire and data were eligible for further analysis. They were from 12 provincial-level administrative regions, among which 7 were in the Northern part of China (including Beijing, Tianjin, Shandong, Hebei, Liaoning, Neimenggu, Jilin) and 5 were in the Southern part of China (including Shanghai, Fujian, Hunan, Jiangsu and Guangdong). Table 1 shows the sociodemographic characteristics of the study participants. The median age of the participants was 40 (36, 45) years, and the majority were female (70.5%). The median professional experience as gastroenterologists was 11 (7, 17) years, while the median experience as endoscopists was 8 (3, 15) years. Most respondents (108, 56%) were IBD subspecialists with a median experience of 5.5 (3, 10) years. Most respondents (103, 53%) had previously received IBD endoscopy screening training (Table 1).

Knowledge of commonly used endoscopic indices in IBD

This part included 10 single choice questions and 4 open answer questions. Table 2 showed the content of the single choice questions and the accuracy rate. The question with the lowest accuracy rate was about the definition of aphthous ulcer (Fig. 1), for which the correct rate was only 11.9%. The median knowledge score was 8 (6, 9) points.

Four nouns with vague or difficult definitions were selected to set open answer questions. The first question was about the definition of deep ulceration. A total of 128 (66.3%) respondents believed that there was no clear

Table 2 Knowledge of commonly used endoscopic indices in IBD

Endoscopic indices knowledge questions	True, *N* (%)
UCEIS	
Definition of vascular pattern	145 (75.1)
Definition of bleeding	144 (74.6)
Definition of erosions and ulcers	113 (58.5)
SES-CD	
Definition of size of ulcers	186 (96.4)
Definition of ulcerated surface	153 (79.3)
Definition of affected surface	162 (83.9)
Definition of presence of narrowings	161 (83.4)
Rutgeerts Postoperative Endoscopic Index	164 (85.0)
Other definition	
Aphthous ulcers	23 (11.9)
Moderate Stenosis	169 (87.6)

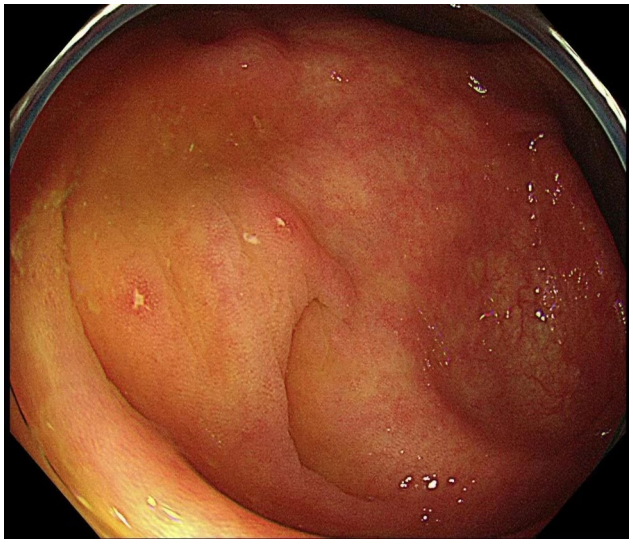

Fig. 1 A typical aphthous ulcer in a CD patient, which was a tiny, flat red lesion with a white center

definition of deep ulcers. Tirty-one (16.1%) respondents believed that deep ulcers were defined as ulcers involving the submucosa or muscular layer, while 10 (5.2%) respondents believed that deep ulcers were defined as ulcers with a diameter greater than 2 centimeters. The second question was about ulcerated surface in SES-CD. A total of 117 (60.6%) respondents believed that the interpretation was not clear or subjective. Seventeen (8.8%) believed that ulcerated surface were the proportion of ulcerated area to the whole intestinal mucosal area, while 10 (5.2%) believed that it was the proportion of the ulcer to the circumferential lumen of the intestine, 5 (2.6%) believed that it was the ratio of the length of the ulcer to the entire intestinal segment. The third question was about the affected surface in SES-CD. A total of 107 (55.4%) respondents believed that the interpretation was not clear or subjective. Twenty-seven (14.0%) believed

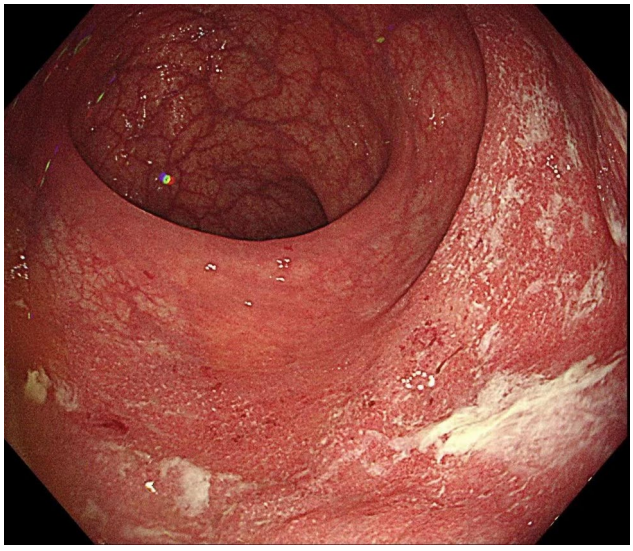

Fig. 2 A typical Mayo Score 2 UC patient, which showed marked erythema, absent vascular pattern, friability and erosions

that the affected surface was defined as the proportion of the affected intestinal segment to the total intestine. The last question was about narrowing SES-CD. Ninety-six (49.7%) respondents thought the definition was vague or subjective. Thirty-four (17.6%) described it as cannot being passed by endoscope, 18 (9.3%) described it as feeling resistance when passed by endoscope, and 15 (7.8%) described it as the diameter of the intestinal cavity being smaller than normal.

Attitudes

Ten questions about physicians' attitudes toward IBD endoscopic indices were included in this part. Regarding the evaluation method for UC, most respondents believed that the UCEIS was the most consistent with clinical activity score (141, 73.1%), while the MMSE was considered to be the hardest to master (105, 54.4%). For the MES, 100 (51.8%) respondents believed that moderate disease (MES 2 points) was the most difficult to score, which means marked erythema, an absent vascular pattern, friability, and erosions (Fig. 2). For the UCEIS, 162 (83.9%) respondents thought that the reason why it was difficult to master was that the endoscopic performance for different intestinal segments was inconsistent, which made it difficult to determine the score. Regarding the evaluation method for CD, most respondents believed that the SES-CD was the most consistent with clinical activity score (115, 59.6%), while the CDEIS was considered to be the hardest to master (79, 40.9%). A total of 107 (55.4%) respondents had difficulty judging ulcerated surfaces, 102 (52.8%) respondents had difficulty judging affected surfaces, 102 (55.4%) respondents had difficulty judging the size of ulcers, 99 (51.3%) respondents had difficulty judging affected surfaces, and 59 (30.6%)

respondents had difficulty judging stenosis. For the Rutgeerts Postoperative Endoscopic Index, 100 (51.8%) respondents believed that the most difficult to score was 2 points, and 129 (66.8%) respondents thought the index was cumbersome to use and hard to remember. Other common factors affecting the evaluation and judgment of endoscopy included training experience (173, 89.6%), the resolution of endoscopic images (142, 73.6%), standard operation during endoscopy (128, 66.3%), previous experience (117, 60.6%) and whether feedback could be received (72, 37.3%).

Practices

In clinical practice, 92 (47.7%) respondents thought that the probability of using endoscopic indices for IBD patients was medium, 47 (24.4%) thought that the probability was low, 34 (17.6%) thought the probability was high, and 20 (10.4%) thought they would never use these indices. The expectation of concordance between endoscopy indices and clinical symptoms, inflammatory markers (e.g., C-reactive protein), and fecal calprotectin are shown in Table 3. IBD subspecialists and gastroenterologists who had previously received IBD endoscopy screening training reported a higher probability of utilizing endoscopic indices for IBD patients ($p<0.001$, $p=0.029$, respectively).

Consistency assessment

The concordance was good-acceptable for most measurements for UC. The intraobserver ICC reliability for the MES was 0.773 (95% CI: 0.539–0.946) before training and increased to 0.861 (95% CI: 0.687–0.969) after training. For the UCEIS, improvement in consistency was shown before and after training, from 0.739 (95% CI: 0.489–0.936) to 0.877 (95% CI: 0.718–0.973). The consistency of the vascular pattern, bleeding and erosions and ulcers all improved after training. The concordance was poor-moderate for the CDEIS among gastroenterologists. The ICC for deep ulcerations was 0.607 (95% CI: 0.276–0.933), for superficial ulceration was 0.391 (95% CI: 0.098–0.864), for surface involved by the disease was 0.514 (95% CI: 0.190–0.908), and for ulcerated surface was 0.640 (95% CI: 0.313–0.941). The ICC reliability for deep ulcerations and superficial ulcerations improved after training, while that for involved surfaces and ulcerated surfaces showed no obvious change and even slightly decline. Rutgeerts score showed the most significant improvement in consistency before and after training, from 0.407 (95% CI: 0.025–0.999) to 0.909 (95% CI: 0.530–1.000). Intraobserver consistency of all indices before and after training were shown in Fig. 3.

Discussion

This was a multicenter cross-sectional study aimed at assessing the level of knowledge, attitudes, and practices of endoscopy among gastroenterologists in the diagnosis and management of IBD. There were important findings, as follows. First, most gastroenterologists were able to select the right answer to knowledge questions, which indicates that it is truly simple. However, the uncertainty of some definitions, including those for deep ulcerations, ulcerated surfaces, affected surfaces and narrowing, led to differences in the interpretation and judgment of results, which suggested that endoscopy indicators need to be defined in a more standardized way. Second, the UCEIS score and SES-CD were considered most consistent with clinical practice in the evaluation of UC and CD, respectively. Third, IBD subspecialists and gastroenterologists who had previously received IBD endoscopy screening training had a higher probability of using endoscopic indices for IBD patients. Finally, training could improve consistency among gastroenterologists in the endoscopic evaluation of UC. These results suggested that some concepts need to be clarified and unified training needs to be provided for gastroenterologists to improve the consistency of interpretation of endoscopic indices to improve clinical practice.

The majority of gastroenterologists were able to accurately select the correct answer to knowledge questions regarding endoscopic indices for IBD, with a median knowledge score of 8 (6, 9) points. The scores might be related to the fact that the respondents were experienced gastroenterologists with a median of 8 years of experience in endoscopy. However, high scores for single-choice questions did not mean that the indices could be easily applied in clinical practice. This study also reflected that some definitions in IBD endoscopy were unclear and confusing. For example, only 11.9% of respondents answered correctly regarding the definition of aphthous ulcers. This result was somewhat surprising because aphthous ulcers are quite common in clinical practice and are clearly defined as tiny (2–3 mm), raised or flat red lesions with a white center [12]. Some participants reported that they confused the definition of aphthous ulcers and erosion, which may partly explain the low correct answer rate.

Table 3 Expectation of concordance between endoscopy indices and clinical indicators

Expectation of compliance between endoscopy indices and	Never considered, *N* (%)	Low, *N* (%)	Medium, *N* (%)	High, *N* (%)
Clinical symptoms	11 (5.7)	21 (10.9)	122 (63.2)	39 (20.2)
C-reactive protein	12 (6.2)	33 (17.1)	109 (56.5)	39 (20.2)
Fecal calprotectin	54 (28)	23 (11.9)	70 (36.3)	46 (23.8)

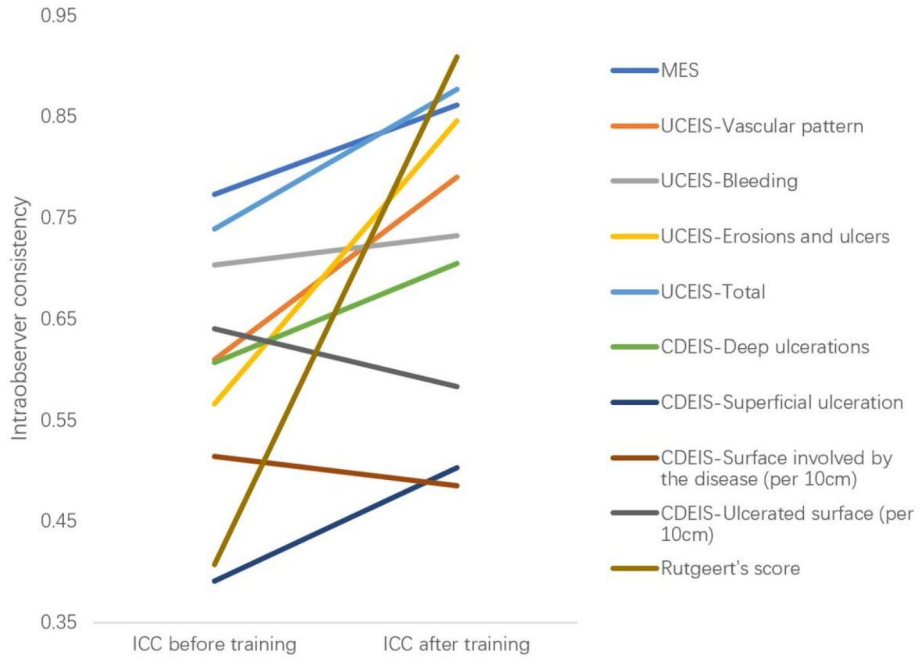

Fig. 3 Intraobserver consistency before and after training
Rutgeerts score showed the most significant improvement in consistency before and after training. For MES and UCEIS, improvement in consistency can be seen before and after training. The ICC reliability for involved surfaces and ulcerated surfaces showed slightly decline before and after training

In open answer questions, over half of the respondents (128, 66.3%) believed that there was no clear definition of deep ulcers. Some respondents believed that deep ulcers were related to ulcer diameter, while others believed that deep ulcers were related to infiltration depth. Since the scoring system of the CDEIS is time-consuming, complicated and not user-friendly, the SES-CD was developed and validated in 2004 [13]. Four endoscopic variables were selected in the SES-CD, including ulcers, the proportion of the surface covered by ulcers, the proportion of the surface with any other lesions, and stenosis. However, a detailed and accurate definition was not given in the original document. Because of the uncertainty of these concepts, gastroenterologists may report different results after endoscopic evaluations, thus affecting the clinical efficacy in clinical trials.

In the analysis of attitudes, most respondents believed that the UCEIS was most consistent with clinical practice for UC. The UCEIS was developed from a two-phase study using video sigmoidoscopies from patients with Mayo Clinic scores ranging from 0 to 11, patients without UC and patients with acute severe UC [14]. Researchers also demonstrated that there was a high level of correlation between UCEIS scores and the overall assessment of severity (correlation coefficient, 0.93). The UCEIS and its components showed satisfactory intrainvestigator and interinvestigator reliability [15]. A recent study also demonstrated that the UCEIS might be superior to the MES because of its accuracy and predictive role in identifying unresponsiveness to therapy [16].

Most respondents believed that the SES-CD was most consistent with clinical practice in the evaluation of CD. Adequate endoscopic scoring in CD patients is crucial but difficult. In clinical practice, the SES-CD is not typically recorded by clinicians in practice or outside of clinical trials. In a recent study, the SES-CD endoscopic prediction model was found to be an effective predictor of intestinal obstruction in patients with CD [17]. Training experience, the resolution of endoscopic images, standard operation during endoscopy, previous experience and whether feedback could be received might affect the results of endoscopic evaluations.

In clinical practice, the probability of using endoscopic indices for IBD patients is not ideal. Approximately 1/3 respondents thought that they would never use these indices or that the probability of using these indices was low. This might be related to the complexity and lack of user-friendly indices, especially indices for the evaluation of CD. We also found that IBD subspecialists and gastroenterologists who had previously received IBD endoscopy screening training had a higher probability of using endoscopic indices for IBD patients. This phenomenon suggested that the more familiar they are with these indices, the more likely they are to use them. Most respondents believed that the endoscopy indices had certain compliance with clinical symptoms, inflammatory markers (e.g., C-reactive protein), and fecal calprotectin.

To make it easier to evaluate the efficacy of CD therapy, researchers are also developing new endoscopic scoring systems, such as the Simplified Endoscopic Mucosal Assessment for Crohn's Disease (SEMA-CD) [18]. The SEMA-CD strongly correlated with the SES-CD and showed good intra- and interoperator reliability.

The consistency of the interpretation of endoscopy indices was different between UC and CD. Intraobserver consistency was higher in the MES and UCEIS than in the CDEIS and Rutgeerts score. Only the accurate interpretation of endoscopic reports can accurately assess disease conditions and guide treatment. The inconsistent interpretation of endoscopic reports among gastroenterologists may affect patients' treatment choices. Our study demonstrated that intraobserver reliability increased dramatically after training, especially in the MES, UCEIS and Rutgeets score. However, the concordance was only moderate or even poor and showed no improvement in CDEIS scores after training. Perhaps the main reason centered on the vague or unclear definitions of concepts in the CDEIS and the difficulty in evaluating involved surfaces or ulcerated surfaces in endoscopic operation. Inconsistency may cause errors and restrict the application of these indices in clinical trials.

Several measures can be taken to improve this phenomenon. First, vague or unclear definitions in endoscopic indices, such as those regarding deep ulcerations, ulcerated surfaces, affected surfaces and narrowing, should be clarified. Second, training in endoscopy should be increased. Currently, a growing awareness of procedural quality and patient safety has spurred the implementation of competency-based education systems [19]. There has been a steady increase in the number of advanced endoscopy applicants and training positions in recent years in America [20]. Due to the increasing prevalence of inflammatory bowel disease and its serious impact on patients' quality of life, we advocate for more IBD endoscopy training programs for gastroenterologists. Third, the interpretation of endoscopic results should be improved. Artificial intelligence (AI) has been examined in the field of inflammatory bowel disease endoscopy with promising data. It is widely used in IBD diagnosis, disease severity grading and remission prediction. AI-driven systems could show comparable performance to scores given by expert endoscopists [21]. AI may improve clinical practice and shape our knowledge in the near future [22].

This study has some limitations. The sample size was small, and the respondents were conveniently sampled rather than randomly sampled; thus, the results might not be able to represent the knowledge, attitudes and practices of all gastroenterologists in China. Training in small groups significantly improves overall consistency of endoscopy indices by gastroenterologist, however each endoscopy score requires training on a larger sample size. In addition, the use of an online questionnaire to collect data has limitations. Therefore, all results are limited to our study participants only, and further research with a larger sample size is needed.

Conclusion

In conclusion, this is the first and largest multicenter, cross-sectional study on the knowledge, attitudes, and practices of endoscopy among gastroenterologists in the diagnosis and management of IBD in China. We found suboptimal knowledge, attitudes, and practices regarding the use of endoscopic indices in China. Some concepts in endoscopic indices were vague, including those regarding deep ulcerations, ulcerated surfaces, affected surfaces and narrowing, which may cause errors and restrict the application of these indices in clinical trials. The consistency was higher in endoscopic indices for UC than for CD, and intraobserver reliability increased dramatically after training, especially for MESs, UCEIS scores and Rutgeets scores. We advocate for the clarification of vague or unclear definitions in endoscopic indices, increasing training and using new technology such as AI to improve the interpretation of endoscopic results to enhance the application of endoscopic evaluations and endoscopic indices in clinical practice.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-024-03436-z.

Supplementary Material 1

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Author contributions

Yinghao Sun: Study design, Data analysis, Writing-Original Draft. Gechong Ruan: Data Curation, Writing-Review & Editing. Xiaoyin Bai: Study design, Validation. Wei Han: Methodology, Investigation. Minglan Yang: Methodology, Investigation. Lixin Jin: Methodology, Investigation. Yanni Huang: Methodology, Investigation. Xiaoxia Hou: Methodology, Investigation. Ke Shu: Methodology, Investigation. Yingying Liu: Methodology, Investigation. Yafeng Lu: Methodology, Investigation. Yan Zhao: Methodology, Investigation. Jie Zhong: Supervision. Hong Yang: Methodology, Supervision, Writing-Review & Editing.

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Data availability

The datasets generated and analysed during the current study are not publicly available due to ethical limitations but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Committee of Peking Union Medical College Hospital (No. I-23ZM0023). The consent obtained from all participants was informed.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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