THERAPEUTIC ADVANCES in
Gastroenterology

Original Research

Geographical heterogeneity in the disease characteristics and management of patients with inflammatory bowel disease, the preliminary results of a Chinese database for IBD (CHASE-IBD)

Ther Adv Gastroenterol

2023, Vol. 16: 1–14

DOI: 10.1177/17562848231210367

Jian Wan, Jun Shen, Xiaoping Wu, Jie Zhong, Yan Chen, Lanxiang Zhu, Yinglei Miao, Naizhong Hu, Jie Chen, Jie Liang and Kaichun Wu

Abstract

Background: The incidence of inflammatory bowel disease (IBD) is rapidly increasing in China, a vast country with significant geographical differences. The socioeconomic status of Eastern China is significantly higher than that of Western China.

Objectives: This study aimed to describe the geographical heterogeneity in the characteristics and management of patients with IBD in both Eastern and Western China.

Design: This was a multicenter, cross-sectional study.

Methods: Patients with IBD with ages ⩾18 years up to 18 January 2023 were included in the analysis from the Chinese database for IBD. Logistic regression was used to identify risk factors associated with surgeries among patients with IBD.

Results: Among 8305 patients with IBD, the ratio of ulcerative colitis (UC) to Crohn's disease (CD) was 4.13 and 0.33 in Western and Eastern China, respectively. The median age at diagnosis of UC and CD was 40.69 and 28.58 years, respectively. There was a male predominance among patients with UC (54.3%) and CD (68.0%). The two regions exhibited a similar distribution of disease locations in UC. However, Western China had a higher proportion of L2 involvement (30.0% *versus* 19.1%) and more advanced disease behavior (B2 and B3) (48.8% *versus* 39.8%) than Eastern China. Patients with IBD in Western China received more 5-aminosalicylic acid and corticosteroids and fewer immunomodulators and biologicals. In terms of surgical risk, Eastern China [*versus* Western China, odds ratios (OR): 5.36, 95% confidence intervals (CI): 2.96–9.68] was associated with a higher risk of surgery in UC, while Western China (*versus* Eastern China, OR: 3.39, 95% CI: 2.37–4.86) was associated with a higher risk of surgery in CD.

Conclusion: Geographical heterogeneity exists in the disease characteristics and management of IBD in Eastern and Western China. These findings have the potential to guide the formulation of location-specific strategies aimed at enhancing the long-term outcomes of patients with IBD.

Keywords: China, geographical heterogeneity, inflammatory bowel disease, surgery

Received: 24 June 2023; revised manuscript accepted: 11 October 2023.

Correspondence to:
Kaichun Wu
State Key Laboratory of Holistic Integrative Management of Gastrointestinal Cancers and National Clinical Research Center for Digestive Diseases, Xijing Hospital of Digestive Diseases, Fourth Military Medical University, 127 Changle West Road, Xi'an, Shaanxi 710032, China
kaicwu@fmmu.edu.cn

Jian Wan
Jie Liang
State Key Laboratory of Holistic Integrative Management of Gastrointestinal Cancers and National Clinical Research Center for Digestive Diseases, Xijing Hospital of Digestive Diseases, Fourth Military Medical University, Xi'an, Shaanxi, China

Jun Shen
Department of Gastroenterology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Institute of Digestive Disease, Shanghai, China

Xiaoping Wu
Department of Gastroenterology, The Second Xiangya Hospital of Central South University, Changsha, Hunan, China

Jie Zhong
Department of Gastroenterology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Yan Chen
Center of Inflammatory Bowel Disease, Department of Gastroenterology, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China

Lanxiang Zhu
Department of Gastroenterology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China

Yinglei Miao
Department of Gastroenterology, The First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, China

Naizhong Hu
Department of Gastroenterology, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China

Jie Chen
Department of Gastroenterology, Northern Jiangsu People's Hospital, Yangzhou, Jiangsu, China

Introduction

Inflammatory bowel diseases (IBDs), including ulcerative colitis (UC) and Crohn's disease (CD), are chronic, nonspecific inflammatory intestinal diseases of unknown etiology characterized by a relapsing and remitting course.[1,2] CD affects any part of the gastrointestinal tract with a progressive and destructive course, whereas UC affects the colon and rectum.[1,2] Approximately 15.6% of patients with UC and 46.6% of patients with CD require surgery because of therapy failure or dysplasia in the 10 years following diagnosis.[1–3]

Although the incidence of IBD is stable in North American and European countries, it is increasing in newly industrialized countries.[4,5] With the development of urbanization and the social economy, its incidence is increasing rapidly in China.[6] It is estimated that there will be 1.5 million patients with IBD in China by 2050.[5] One-third of direct IBD healthcare costs are due to hospitalizations, and surgery is associated with higher hospitalization costs.[3,7] Healthcare systems should be prepared for the increasing number of patients with IBD, as the potential burden of IBD is substantial, especially in areas with high rates of surgery.

China is characterized by great geographical differences in socioeconomic status, healthcare access, industrialization, and urbanization. The distribution of IBD phenotypes and the clinical characteristics of patients with IBD across different geographic locations varied.[8,9] The industrialization and socioeconomic level of the Eastern China is significantly higher than those of the Western China.[10] There is a positive association of the incidence of IBD with gross domestic product (GDP) and east-to-west gradient for IBD with higher incidence in the east.[11] Currently, previous studies describing the characteristics of IBD in China have been constrained to single-center or small-sample studies,[12–15] which precludes a description of the differences in the characteristics of patients with IBD in different regions of China. However, studies with large sample head-to-head comparing the clinical characteristics of IBD across different regions of China are lacking. Heterogeneity in the clinical patterns of IBD might result in the differences in treatment and surgical rates in different regions. Understanding the distribution landscape and clinical characteristics of IBD across different regions of China is essential for improving the management and disease outcomes of patients with IBD.

In this study, the Chinese database for IBD (CHASE-IBD) was used to comprehensively describe and compare the clinical characteristics of patient with IBD from different regions of China, evaluate the prevalence, and identify associated risk factors for surgery in patients with IBD. The results can provide comprehensive data analysis to develop strategies for optimal healthcare services for the growing number of patients with IBD in China.

Methods

Chinese database for IBD

The objectives of the CHASE-IBD are to effectively and systematically organize large amounts of data on patients with IBD, improve the management effectiveness of long-term follow-up and surveillance of response to therapy in patients with IBD, and provide data support for clinical and basic research on IBD. The CHASE-IBD was established in March 2018 and was first used in five hospitals in Shanghai, China. In March 2019, the database was approved and owned by the IBD Group, the Chinese Society of Gastroenterology, Chinese Medical Association and then was gradually promoted in hospitals across the country.

Data collection. The electronic case report forms of CHASE-IBD were designed to ensure standardization and consistency of data collection. The CHASE-IBD system is maintained by specific personnel, including data processing engineers, doctors, and nurses. Before each hospital integrated the use of the database into their operations, the doctors and nurses of the IBD-specific clinics were trained in the collection and entry of clinical data by the professional staff of CHASE-IBD. Upon approval by the IBD Group, Chinese Society of Gastroenterology, Chinese Medical Association, exclusive accounts granting access to the database are provided to participating hospitals for patient data collection, limited to the clinical data of patients in each hospital. Patients with IBD ages $\geqslant$18 years were prospectively enrolled in the CHASE-IBD cohort when they visited the IBD-specific clinics at each hospital. Patients aged $<$18 years old were enrolled into a pediatric database. The clinical data of patients with IBD who were diagnosed before the clinic participated in the database were collected retrospectively from electronic medical records. A dedicated data

collector performed data collection at the time of enrollment and all subsequent clinic visits or hospitalizations and then recorded the data on a dedicated website using the standardized electronic case report forms.

Data captured into the database included demographic data, IBD diagnosis, time of diagnosis, extra-intestinal manifestations (EIMs), Montreal classification phenotype, disease activity scores, medication history, surgical records, and related laboratory, radiographic, and endoscopic findings. The diagnosis and treatment of IBD were based on the Chinese consensus on the diagnosis and treatment of IBD, which was similar to the European Crohn's and Colitis Organization (ECCO) consensus.[16,17]

Data archiving and quality maintenance. Patients with IBD were referred to IBD specialists or IBD-specific clinics for regular follow-ups at each participating site. The unique 18-digit ID number assigned to all Chinese citizens at birth facilitated comprehensive follow-up of these patients across the participating hospitals. The data were updated at each collection, which allowed for longitudinal follow-up. The clinical data of patients with IBD are stored in a central database accessible through a secure network using encrypted connections. The CHASE-IBD methodology prioritizes data quality, incorporating systematic reviews by database professionals, regular site principal investigator meetings at the Congress of Gastroenterology China, and conferences organized by the IBD Group, Chinese Society of Gastroenterology, Chinese Medical Association. Only the hospitals certified by the IBD Group, Chinese Society of Gastroenterology, Chinese Medical Association in terms of adhering to standardized procedures for the diagnosis and treatment of IBD can use the database for the follow-up and management of patients with IBD through the website (http://www.chaseibd.com/). Any patient without a confirmed diagnosis of IBD was temporarily recruited to a subset of the database and marked as having a suspected IBD. Suspected patients were moved to the IBD subset only if they had a confirmed diagnosis of IBD and were removed from the database if they were confirmed as non-IBD, ensuring data accuracy and integrity.

Data retrieval, extraction, and protection. Structured query language was used to extract clinical data from the standardized electronic case report forms. De-identified data were obtained only after an investigator submitted a protocol for approval from the IBD Group, Chinese Society of Gastroenterology, Chinese Medical Association. For data protection, the exclusive account of the database of each participating site for data collection can only access the clinical data of the patients in its hospital. All data transmissions were carried out over encrypted Internet connections (the Hypertext Transfer Protocol Secure over Secure Socket Layer) for security.

Study design

This was a cross-sectional study included patients with IBD from the CHASE-IBD database until 18 January 2023. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology statement.[18] This study was approved by the IBD Group, the Chinese Society of Gastroenterology, Chinese Medical Association, and de-identified clinical data of patients with IBD were provided by the CHASE-IBD. When the clinical data on a variable were available for more than 50% of patients, the variable was included in the analysis in this study. The patients included in this study had a confirmed diagnosis of IBD after multiple follow-ups, and only the final diagnostic information was extracted. Only clinical data at the enrollment were analyzed in this study, including demographic data, IBD diagnosis, year of diagnosis, EIM at any time following IBD diagnosis until before recruitment, Montreal classification phenotype, treatments, and surgical history.

Definition. According to the Montreal classification,[19] UC phenotypes include proctitis (E1), left-sided colitis (E2), and extensive colitis (E3). In patients with CD, disease location (L) included ileal (L1), colonic (L2), ileocolonic (L3), and upper gastrointestinal diseases (L4). Disease behavior (B) included B1 (nonstricturing, nonpenetrating), B2 (stricturing), and B3 (penetrating). Perianal disease was identified in patients with CD who had experienced at least one episode of a perianal fistula and/or abscess. Surgery was defined as any IBD-related surgery involving bowel resection. Due to the small number of patients treated with small-molecule drugs, we classified small-molecule drugs as biologics for statistical analysis.

Classification. Mainland China was divided by administrative divisions into seven geographic areas.[20] The socioeconomic level of east, south, north, and central areas of China is significantly higher than those of southwest, northwest, and northeast areas of China.[10] Notably, Beijing, the capital of China, is the political, financial, and cultural center of China, so it is not representative of north area, and only seven patients were included in Beijing. Hebei Province, with a low per-capita GDP, is more representative of north area of China. Then, all the administrative provinces (autonomous regions and centrally administered municipalities) in the analysis were classified into two groups: Eastern China [comprising east area (Anhui, Fujian, Jiangsu, Shandong, Shanghai, and Zhejiang), south area (Guangdong), and central area (Hubei and Hunan)] and Western China [southwest area (Sichuan and Yunnan), northwest area (Shaanxi), northeast area (Liaoning), and north area (Beijing and Hebei)] based on the economic development indicators[10,21] by a cutoff of $10,000 in GDP per capita of the seven geographic areas in China[20] (https://data.stats.gov.cn/) (Supplemental Table 1).

Outcomes. The primary endpoint of this study was to describe the geographical heterogeneity of the characteristics and management in a large cohort of patients with IBD in Eastern and Western China. Secondary endpoints were the prevalence of and risk factors for patients with IBD in China.

Statistical analysis

Data analysis was conducted using the SPSS 26.0 (IBM, Armonk, NY, USA) for Windows. Not available data were defined as the related data were not reported or the specific outcome was not tested at enrollment. Quantitative variables were summarized as the median and interquartile ranges (IQR) and were compared using the *t*-test or Mann–Whitney *U* test, as appropriate. Categorical variables were expressed as frequency and percentage (%) and were compared using the chi-square or Fisher's exact test, as appropriate. Descriptive analyses were based on patients with available data, and the percentage of categorical variables was calculated using the number of patients with available data as the denominator. Logistic regression was used to identify the risk factors associated with surgery in patients with IBD. Significant factors ($p < 0.10$) in the univariate analysis were included in the final logistic regression model. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to quantify the associations between factors and each outcome. All the *p*-values were two-sided, and $p < 0.05$ was considered statistically significant.

Result

Overall, 8305 patients with IBD [UC: 3140 (37.8%); CD: 5077 (61.1%); IBD-U: 88 (1.1%)] were enrolled from 33 tertiary hospitals across 15 provinces, autonomous regions, and centrally administered municipalities. Among these, 25 hospitals were located in 9 provinces (autonomous regions, centrally administered municipalities) of Eastern China and eight hospitals in six provinces (autonomous regions, centrally administered municipalities) of Western China. Western China exhibited a higher proportion of patients with UC, while patients with CD were more prevalent in Eastern China. The ratio of UC to CD was 4.13 and 0.33 in Western and Eastern China, respectively (Supplemental Table S1; Figure 1). The characteristics of the patients with UC and CD are summarized in Table 1. The median age at diagnosis was younger in patients with CD (28.58, IQR: 21.93–37.92) than that in patients with UC (40.69, IQR: 30.04–53.35, $p < 0.001$). The disease duration at enrollment was longer in patients with CD (median: 1.44, IQR: 0.13–4.88) than that in patients with UC (median: 1.18, IQR: 0.09–4.05, $p < 0.001$). The proportion of females in patients with CD (32.0%) was lower than that in patients with UC (45.7%, $p < 0.001$). The proportion of presenting EIM presenting in patients with CD (16.3%) was higher than that in patients with UC (7.8%, $p < 0.001$). Regarding treatment patterns, patients with CD received a higher proportion of immunomodulators (23.4% *versus* 3.7%, $p < 0.001$) and biologicals (37.0% *versus* 7.4%, $p < 0.001$) and a lower proportion of 5-aminosalicylic acid (5-ASA) (28.0% *versus* 85.7%, $p < 0.001$) than patients with UC. No significant difference was observed in the proportion of corticosteroid use between the two groups ($p = 0.110$).

Geographical differences in the characteristics of patients with UC

Table 2 and Figure 2(a) show the characteristics of the patients with UC across different regions of

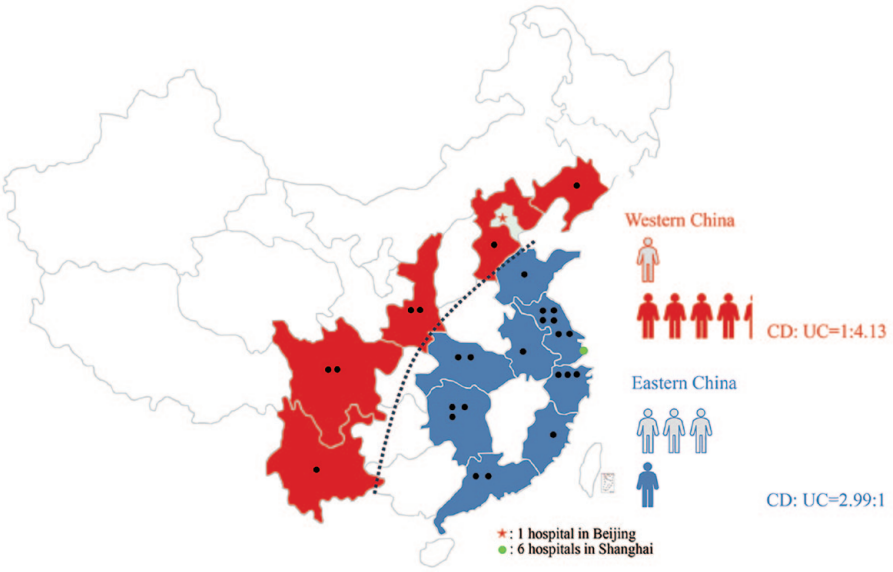

Figure 1. The distribution of hospitals and the ratio of UC to CD in different regions. A black dot represents a hospital.
CD, Crohn's disease; UC, ulcerative colitis.

China. In Western China, patients with UC exhibited a younger median age at diagnosis (39.56 years *versus* 42.48 years), along with a younger median disease duration at enrollment (1.88 years *versus* 0.66 years) compared to Eastern China (all $p < 0.001$). Regarding treatment patterns [Figure 2(d)], patients with UC in Western China received a higher proportion of 5-ASA (94.5% *versus* 77.0%, $p < 0.001$) and corticosteroids (18.6% *versus* 15.8%, $p = 0.003$) and a lower proportion of immunomodulators (2.7% *versus* 4.6%, $p = 0.003$) than patients in Eastern China. No significant differences were observed in the use of biologicals, prevalence of female sex, disease locations, or EIM (all $p > 0.05$).

Geographical differences in the characteristics of patients with CD

Table 3 and Figure 2(b) and (c) showed the characteristics of patients with CD in different regions of China. The median disease duration at enrollment (1.88 years *versus* 0.66 years) was longer in patients with CD in Western China than that in Eastern China ($p = 0.019$). Higher proportions of EIM (26.1% *versus* 15.2%, $p < 0.001$) and females (39.7% *versus* 31.4, $p = 0.001$) were observed in Western China compared to Eastern China. Notably, the distribution pattern of disease location and behavior at enrollment differed among the different regions of China ($p < 0.001$). The proportions of patients with L1, L2, L3, and L4 were 21.9%, 30.0%, 42.8%, and 5.3%, respectively, in Western China and 29.5%, 19.1%, 41.6%, and 9.8%, respectively, in Eastern China. The proportions of patients with B1, B2, and B3 were 51.2%, 39.9%, and 8.8% in Western China and 60.2%, 27.8%, and 12.0% in Eastern China, respectively. The proportion of patients with perianal disease was lower in Western China than in Eastern China (9.5% *versus* 15.1%, $p = 0.003$). Regarding treatment patterns [Figure 2(e)], patients with CD in Western China received a higher proportion of 5-ASA (46.6% *versus* 26.5%) and corticosteroids (24.7% *versus* 15.2%) and a lower proportion of immunomodulators (14.7% *versus* 24.1%) and biologicals (26.8% *versus* 37.9%) than patients from Eastern China (all $p < 0.001$). The median age at diagnosis was not significantly different between the two regions ($p > 0.05$).

Prevalence and risk factors of surgery

The proportion of patients with CD who underwent surgery was higher than that of patients with UC (12.1% *versus* 2.1%, $p < 0.001$). The surgical rate in patients with UC from Western China was lower than those from Eastern China (1.3% *versus* 2.9%, $p = 0.001$). In contrast, the surgical rate of

Table 1. The characteristics of patients with UC and CD.

Characteristics	UC	CD	*p*-Value
Number of patients, *n* (%)	3140 (38.2)	5077 (61.8)	–
Female, *n* (%)	1435 (45.7)	1625 (32.0)	<0.001
Age at diagnosis, median (IQR)	40.69 (30.04–53.35)	28.58 (21.93–37.92)	<0.001
Disease duration, median (IQR)	1.18 (0.09–4.05)	1.44 (0.13–4.88)	0.001
EIM, *n* (%)	152/1955 (7.8)	451/2772 (16.3)	<0.001
Disease location, *n* (%)			
N (UC)	1818		
E1	478 (26.3)		
E2	642 (35.3)		
E3	698 (38.4)		
N (CD)		2918	
L1		840 (28.8)	
L2		588 (20.2)	
L3		1217 (41.7)	
L4 involvement		273 (9.4)	
Disease behavior (CD), *n* (%)			
N		2918	
B1		1732 (59.4)	
B2		845 (29.0)	
B3		341 (11.7)	
Perianal disease, *n* (%)		747 (14.7)	
Treatments			
5-ASA	2691 (85.7)	1420 (28.0)	<0.001
Corticosteroid	540 (17.2)	806 (15.9)	0.110
Immunomodulator	115 (3.7)	1190 (23.4)	<0.001
Biologicals	233 (7.4)	1881 (37.0)	<0.001
Infliximab	127 (4.0)	1387 (27.3)	–
Adalimumab	4 (0.1)	283 (5.6)	–
Vedolizumab	93 (3.0)	66 (1.3)	–
Ustekinumab	6 (0.2)	161 (3.2)	–
Tofacitinib	3 (0.1)	1 (0.0)	–
Surgery, *n* (%)	66 (2.1)	613 (12.1)	<0.001

5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; EIM, extra-intestinal manifestation; IQR, interquartile ranges; *N*, number of patients for which data are available; UC, ulcerative colitis.

Table 2. The characteristics of patients with UC in different regions of China.

Characteristics	Eastern China	Western China	*p*-Value
Number of patients, *n* (%)	1572 (50.1)	1568 (49.9)	–
Female, *n* (%)	729 (46.4)	706 (45.0)	0.448
Age at diagnosis, median (IQR)	42.48 (30.48–55.85)	39.56 (29.58–51.39)	<0.001
Disease duration, median (IQR)	0.66 (0.03–3.36)	1.88 (0.35–4.75)	<0.001
EIM, *n* (%)	41/607 (6.8)	111/1348 (8.2)	0.258
Disease location, *n* (%)			
N	579	1239	0.203
E1	138 (23.8)	340 (27.4)	
E2	205 (35.4)	437 (35.3)	
E3	236 (40.8)	462 (37.3)	
Treatments			
5-ASA	1210 (77.0)	1481 (94.5)	<0.001
Corticosteroid	249 (15.8)	291 (18.6)	0.044
Immunomodulator	73 (4.6)	42 (2.7)	0.003
Biologicals	130 (8.3)	103 (6.6)	0.069
Infliximab	80	47	
Adalimumab	3	1	
Vedolizumab	41	52	
Ustekinumab	3	3	
Tofacitinib	3	0	
Surgery, *n* (%)	46 (2.9)	20 (1.3)	0.001

5-ASA, 5-aminosalicylic acid; EIM, extra-intestinal manifestations; IQR, interquartile ranges; N, number of patients for whom data were available; UC, ulcerative colitis.

patients with CD is higher in Western China than in Eastern China (25.3% *versus* 11.1%, $p<0.001$). The univariate analyses of the risk factors associated with surgery in patients with UC and CD are shown in Supplemental Tables 3 and 4. Multivariate analyses results are presented in Table 4. For patients with UC, disease duration (OR: 1.09, 95% CI: 1.05–1.12, $p<0.001$), Eastern China (*versus* Western China, OR: 5.36, 95% CI: 2.96–9.68, $p<0.001$), and E3 (OR: 4.57, 95% CI: 1.76–11.85, $p=0.002$) were risk factors for surgery. For patients with CD, age at diagnosis (OR: 1.03, 95% CI: 1.02–1.04, $p<0.001$), disease duration (OR: 1.08, 95% CI: 1.05–1.11, $p<0.001$), Western China (*versus* Eastern China, OR: 3.39, 95% CI: 2.37–4.86, $p<0.001$), L3 (OR: 1.39, 95% CI: 1.03–1.86, $p=0.031$), B2 (OR: 2.81, 95% CI: 2.11–3.75, $p<0.001$), and B3 (OR: 15.67, 95% CI: 11.36–21.61, $p<0.001$) were significantly associated with surgery.

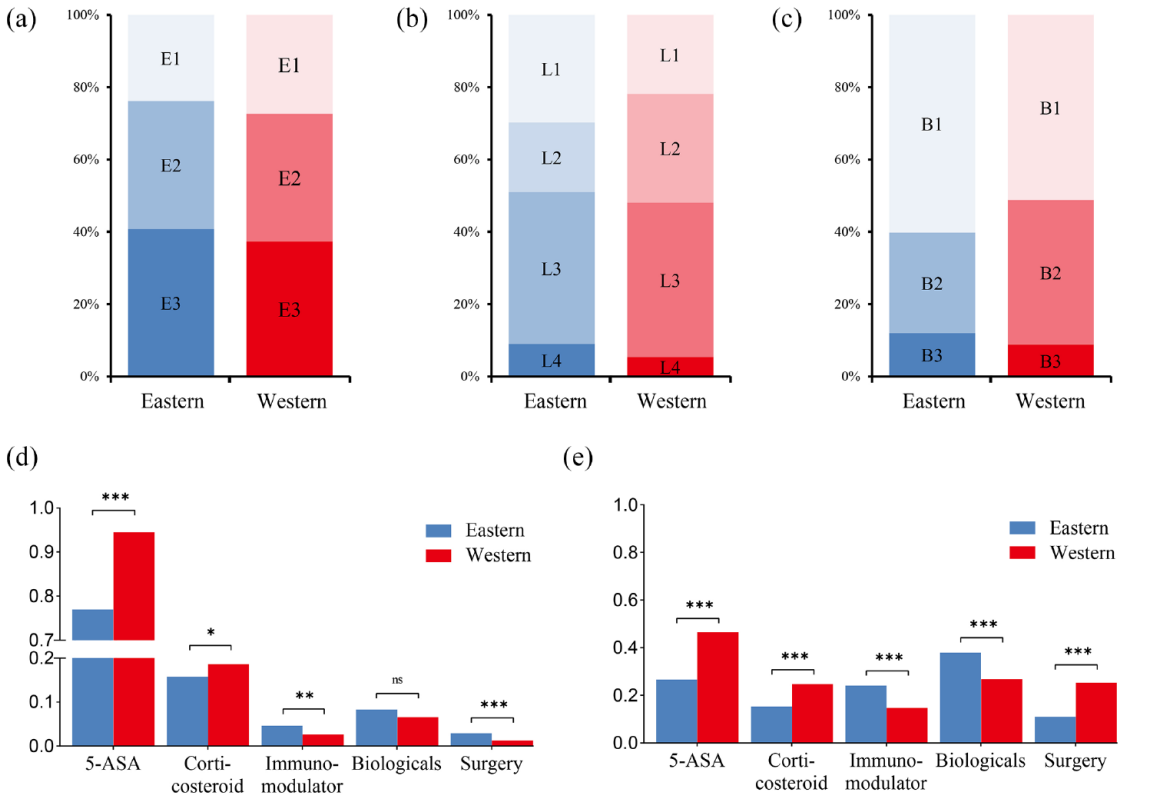

Figure 2. (a) Disease location of UC, (b) disease location of CD, (c) disease behavior of CD, (d) treatment of UC, and (e) treatment of CD in different regions.
CD, Crohn's disease; UC, ulcerative colitis.

Discussion

This was the largest multicenter study to characterize patients with IBD across different geographical regions of China, including the clinical features, treatment patterns, and surgical rates. Notably, CD exhibited a higher prevalence in Eastern China, whereas UC was more prevalent in Western China. The surgical rate was higher in Eastern China for patients with UC and in Western China for patients with CD. Understanding the distribution and clinical features of IBD in different regions of China is crucial for improving long-term outcomes of patients with IBD.

In Asia, the incidence of both UC and CD has increased rapidly, whereas, in more developed countries, the increasing rate of CD is steeper, resulting in a reduction in the ratio of UC to CD over time.[22] This pattern seems to be mirrored in China,[21] a vast country marked by varying economic development in the Eastern and Western China. Although a direct comparison of IBD prevalence across regions was hindered due to increased participation from Eastern China in the CHASE-IBD study, we were able to identify the predominant IBD subtype and the ratio of UC to CD in different regions. Our findings demonstrated variability in the UC-to-CD ratio within different Chinese regions; the number of patients with CD in Eastern China was higher than that of patients with UC, whereas the reverse was true for Western China. There was an east-to-west gradient for IBD with higher incidence in the east.[11] In regions with a high incidence of IBD, the incidence of both diseases seemed to be stabilized, with the incidence of CD often surpassing UC.[6] In the past, UC was more common than CD in China,[22] even in more developed regions such as Wuhan and Zhongshan in Eastern China.[13,23] However, over the last decade, a reverse trend emerged in the developed regions of China, such as East, South, and Central China. The incidence of UC in China is similar to the highest incidence of IBD reported in East Asia.[21] UC remains the predominant disease in nondeveloped regions, such as the north and west areas

Table 3. The characteristics of patients with CD in different regions of China.

Characteristics	Eastern China	Western China	*p*-Value
Number of patients, *n* (%)	4697 (92.5)	380 (7.5)	–
Female, *n* (%)	1474 (31.4)	151 (39.7)	0.001
Age at diagnosis, median (IQR)	28.53 (22.00–37.60)	29.94 (21.27–41.92)	0.375
Disease duration, median (IQR)	1.35 (0.12–4.47)	1.85 (0.29–5.01)	0.019
EIM, *n* (%)	379/2496 (15.2)	72/276 (26.1)	<0.001
Disease location, *n* (%)			
N	2635	283	<0.001
L1	778 (29.5)	62 (21.9)	
L2	503 (19.1)	85 (30.0)	
L3	1096 (41.6)	121 (42.8)	
L4 involvement	258 (9.8)	15 (5.3)	
Disease behavior (CD), *n* (%)			
N	2635	283	<0.001
B1	1587 (60.2)	145 (51.2)	
B2	732 (27.8)	113 (39.9)	
B3	316 (12.0)	25 (8.8)	
Perianal disease, *n* (%)	711 (15.1)	36 (9.5)	0.003
Treatments			
5-ASA	1243 (26.5)	177 (46.6)	<0.001
Corticosteroid	712 (15.2)	94 (24.7)	<0.001
Immunomodulator	1134 (24.1)	56 (14.7)	<0.001
Biologicals	1779 (37.9)	102 (26.8)	<0.001
Infliximab	1321 (28.1)	66 (17.4)	
Adalimumab	277 (5.9)	6 (1.6)	
Vedolizumab	61 (1.3)	5 (1.3)	
Ustekinumab	133 (2.8)	28 (7.4)	
Tofacitinib	1 (0.0)	0 (0.0)	
Surgery, *n* (%)	517 (11.0)	96 (25.3)	<0.001

5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; EIM, extra-intestinal manifestations; IQR, interquartile ranges; *N*, number of patients for which data are available.

Table 4. Multivariate analyses for the risk factors of surgery in patients with UC and CD.

Characteristics	OR (95% CI)	*p* Value
UC		
Disease duration (per 1 year)	1.09 (1.05–1.12)	<0.001
Regions		<0.001
Western China	Ref	
Eastern China	5.36 (2.96–9.68)	
Disease location		0.001
E1	Ref	
E2	2.17 (0.78–6.03)	0.138
E3	4.57 (1.76–11.85)	0.002
5-ASA	0.80 (0.41–1.56)	0.505
CD		
Age at diagnosis (per 1 year)	1.03 (1.02–1.04)	<0.001
Disease duration (per 1 year)	1.08 (1.05–1.11)	<0.001
Regions		<0.001
Eastern China	Ref	
Western China	3.39 (2.37–4.86)	
Disease location		0.028
L1	Ref	
L2	0.98 (0.65–1.47)	0.910
L3	1.39 (1.03–1.86)	0.031
L4 involvement	1.02 (0.67–1.56)	0.911
Disease behavior		<0.001
B1	Ref	
B2	2.81 (2.11–3.75)	<0.001
B3	15.67 (11.36–21.61)	<0.001
5-ASA	0.98 (0.70–1.36)	0.888
Immunomodulator	1.30 (0.93–1.81)	0.125
Biologicals	1.29 (0.95–1.75)	0.104

5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; CI, confidence interval; OR, odds ratio; UC, ulcerative colitis.

China. Over the past decade, there has been growing awareness of UC, while awareness of CD needs to be strengthened. The lack of awareness of CD in some underdeveloped areas of China can easily lead to missed diagnoses in patients with CD. Clinicians should recognize the increasing burden of CD and prepare for the better management of patients with CD. Policymakers should implement strategies to improve access to healthcare support by IBD specialists and effective medicines and maximize the outcome of IBD across regions.

In terms of disease characterization, the median age at CD diagnosis was notably lower than that for UC, consistent with previous studies in China.[12,13,23–25] The median age at diagnosis for patients with UC (40.69 years) seemed to be older than that in Europe (median: 37; IQR: 27–55 years),[26] while the median age at diagnosis for patients with CD (28.58 years) seemed to be younger than that in Europe (median: 33; IQR: 23–49 years).[27] The median age at diagnosis for patients with UC and CD was younger than previous studies,[12,23,25] but similar to the results of a recently published study in China.[24] This indicates that the age at diagnosis of patients with IBD in China is gradually decreasing. Additionally, the median disease duration was shorter in this study. The reason for this might be that only the information of the study patients at enrollment was analyzed in our study. A male preponderance of CD and an equal or slight male preponderance of UC were observed in our study, which was similar to previous studies in China.[28,29] Possible reasons include different genetic predispositions and men having a greater opportunity to seek education or jobs in industrialized areas at a younger age, which increases potential environmental risk factors in their early life.[22,28]

Regarding disease patterns, the proportions of patients with E1, E2, and E3 UC were 26.3%, 35.3%, and 38.4%, respectively, and no significant differences were found between Eastern and Western China. The disease location for UC was comparable between our study and Western populations,[26,30] with roughly equal proportions of E1, E2, and E3. However, the proportion of E3 was less than that (47.1%) in a recently published multicenter study in China,[24] possibly because this was a follow-up study with a longer disease duration in

patients with UC than that in our study. For patients with CD, L3 and B1 were the most frequent disease locations and behaviors, similar to other cohorts in Asia.[24,28,31,32] In addition, heterogeneity in the distribution of disease location and behavior was observed between Eastern and Western China. The proportions of L1 and L4 in Eastern China were higher than in Western China, whereas the proportion of L2 was lower. Disease behavior is an important clinical characteristic because it is a risk factor for surgery in patients with CD.[27,28] A higher proportion of more advanced disease behaviors (B2 and B3) was found in Western China, which might explain the higher surgical rate in patients with CD in this region.

Treatment patterns were also significantly different between Eastern and Western China. The proportion of 5-ASA and corticosteroid use was higher in Western China in both patients with UC and CD than in Eastern China, whereas the reverse was true for the use of biologicals. Although 5-ASA is not recommended for the treatment of CD in the ECCO guidelines owing to its controversial efficacy,[33] up to 28% of CD patients were still treated with ASA. It is worth noting that this, in compliance with the guidelines, was more common in Western China, where almost half of the patients with CD were still treated with 5-ASA. There are two possible explanations for this discrepancy in the treatment patterns. First, biological treatment is expensive, and more patients in less developed regions cannot afford it. This could influence the treatment decisions of patients with IBD in China. Consequently, cheaper treatments such as 5-ASA and corticosteroids are more widely used in Western China. Second, it has been reported that the use of 5-ASA can improve the long-term outcomes of patients with CD with colon involvement.[15] Patients with colonic CD are sometimes treated with 5-ASA when they cannot afford the expensive cost of biologics. The proportion of L2 was higher in Western China than that in Eastern regions, which might have resulted in the higher use of 5-ASA in Western China. Interestingly, it has been reported that biological use is associated with a lower disease behavior progression rate.[34,35] Whether the lower proportion of biological usage in Western China leads to higher advanced disease behavior rates (B2 and B3) warrants further research.

Our study highlights multiple risk factors for surgery in patients with UC, such as disease duration, disease location, and no 5-ASA exposure, and in patients with CD, such as age at diagnosis, disease duration, disease location, and disease behavior, as reported in previous studies.[27,28,35–38] Lower rates of UC surgery and higher rates of CD surgery have been observed in Western China. One possible explanation may be the difference in the clinical characteristics of the patients in the two regions. Notably, we also found that geographic location was an independent risk factor for surgery in patients with IBD in multivariate analysis, taking clinical characteristics into consideration. Regional differences in surgical rates cannot be explained by differences in clinical characteristics alone. Other regional factors might contribute to these differences, such as socioeconomic factors, diet, genetic susceptibility, health resources, attitudes toward surgery, and the availability of treatments. Understanding these complexities will be instrumental in effectively addressing region-specific risk factors for surgery in patients with IBD.

Our study has some limitations. First, there was a potential selection bias in this multicenter tertiary hospital-based study, which might have been due to the nature of the non-population-based study and the differing number of enrolled hospitals between the two regions. This makes it impossible to calculate the ratio of UC to CD on a national scale. Second, some potential factors were not included in our study because of insufficient data, such as C-reactive protein level, smoking status, and histological inflammation score. Third, the use of the records in a database could potentially lead to missing data, inaccurate data, and underreporting of outcomes. Only data available for more than 50% of the patients with IBD were analyzed in our study to reduce potential confounding factors. Data entry training, background monitoring of data quality, and regular meetings were conducted to minimize the possibility of inaccurate data. Fourth, resident status data were not available in the database, and we could not distinguish between rural and urban patients. In addition, only the data at enrollment were analyzed, and the long-term outcomes of patients with IBD could not be analyzed. Further studies are required to describe the long-term course of these natural diseases.

In conclusion, the CHASE-IBD database was used to analyze the discrepancies in clinical characteristics and management in different regions of China. The results enhance our awareness of the geographic heterogeneity of IBD in China and could help policymakers in strategies planning by geographic locations to improve the long-term outcomes of patients with IBD in China.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of Xijing Hospital affiliated to the Fourth Military Medical University with approval for all hospitals involved in the study (approval number: KY20232129). The requirement for patient-informed consent was waived by the ethical committee of Xijing Hospital affiliated to the Fourth Military Medical University as there was no identifiable patient information.

Consent for publication

Not applicable.

Author contributions

Jian Wan: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing – original draft.

Jun Shen: Data curation.

Xiaoping Wu: Data curation.

Jie Zhong: Data curation.

Yan Chen: Data curation.

Lanxiang Zhu: Data curation.

Yinglei Miao: Data curation.

Naizhong Hu: Data curation.

Jie Chen: Data curation.

Jie Liang: Validation; Writing – review & editing.

Kaichun Wu: Conceptualization; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Writing – review & editing.

Acknowledgements

We all thank the other investigators in the CHASE-IBD study: Wensong Ge (Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine), Hongjie Zhang (First Affiliated Hospital of Nanjing Medical University), Xin Liu (Second Affiliated Hospital of Xi'an Jiaotong University), Xiaoqi Zhang (The Affiliated Nanjing Drum Tower Hospital of Medical School of Nanjing University), Xiaolan Zhang (The Second Hospital of Hebei Medical University), Zhongsheng Xia (Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University), Jianjiong Wu (Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine), Fanda Chen (Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine), Qunyan Zhou (the Affiliated Wuxi People's Hospital, Nanjing Medical University), Xiaolin Zhong (Affiliated Hospital of Southwest Medical University), Qi Jiang (Ningbo First Hospital), Jing Yu (the First Affiliated Hospital of Medical College of Shantou University), Yingde Wang (the First Affiliated Hospital of Dalian Medical University), Mei Ye (Zhongnan Hospital of Wuhan University), Chengdang Wang (the First Affiliated Hospital of Fujian Medical University), Qian Cao (Sir Run Run Shaw Hospital, College of Medicine Zhejiang University), Liangru Zhu (Union Hospital, Tongji Medical College, Huazhong University of Science and Technology), Jiaming Qian (Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Hongbing Zhou (the Affiliated Zhuzhou Hospital of Xiangya Medical College of Central South University), Yufang Wang (West China Hospital, Sichuan University), Wen Tang (The Second Affiliated Hospital of Soochow University, Xiaoyang Wang (Third Xiangya Hospital of Central South University), Jianfeng Yao (Huadong Hospital Affiliated to Fudan University), Xueliang Jiang (the Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine). We all also thank the staff of the CHASE-IBD.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Natural Science Foundation of China (82273374, 81627807), and Independent Funds of the Key Laboratory (CBSKL2015Z01).

Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

ORCID iDs

Jian Wan https://orcid.org/0000-0001-9941-0576

Jun Shen https://orcid.org/0000-0001-7206-1847

Jie Chen https://orcid.org/0000-0002-8621-1268

Supplemental material

Supplemental material for this article is available online.

References

1. Kobayashi T, Siegmund B, Le Berre C, *et al.* Ulcerative colitis. *Nat Rev Dis Primers* 2020; 6: 74.
2. Roda G, Chien Ng S, Kotze PG, *et al.* Crohn's disease. *Nat Rev Dis Primers* 2020; 6: 22.
3. Frolkis AD, Dykeman J, Negron ME, *et al.* Risk of surgery for inflammatory bowel diseases has decreased over time: a systematic review and meta-analysis of population-based studies. *Gastroenterology* 2013; 145: 996–1006.
4. Alatab S, Sepanlou SG, Ikuta K, *et al.* The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol* 2020; 5: 17–30.
5. Kaplan GG. The global burden of IBD: from 2015 to 2025. *Nat Rev Gastroenterol Hepatol* 2015; 12: 720–727.
6. Zhao J, Ng SC, Lei Y, *et al.* First prospective, population-based inflammatory bowel disease incidence study in mainland of China: the emergence of 'western' disease. *Inflamm Bowel Dis* 2013; 19: 1839–1845.
7. Xu J, Tang M and Shen J. Trends and factors affecting hospitalization costs in patients with inflammatory bowel disease: a two-center study over the past decade. *Gastroenterol Res Pract* 2013; 2013: 267630.
8. Goldis A, Lupusoru R, Gheorghe L, *et al.* Geographic distribution, phenotype and epidemiological tendency in inflammatory bowel disease patients in Romania. *Medicina (Kaunas)* 2019; 55: 704.
9. Zaltman C, Parra RS, Sassaki LY, *et al.* Real-world disease activity and sociodemographic, clinical and treatment characteristics of moderate-to-severe inflammatory bowel disease in Brazil. *World J Gastroenterol* 2021; 27: 208–223.
10. Yang H, Zhou RN, Qian JM, *et al.* [The prevalence of Crohn's disease based on the basic medical insurance system for urban employees in China in 2013]. *Zhonghua Yi Xue Za Zhi* 2020; 100: 2861–2866.
11. Ng SC, Kaplan GG and Tang W, *et al.* Population density and risk of inflammatory bowel disease: a prospective population-based study in 13 countries or regions in Asia-Pacific. *Am J Gastroenterol* 2019; 114: 107–115.
12. Zhai H, Liu A, Huang W, *et al.* Increasing rate of inflammatory bowel disease: a 12-year retrospective study in NingXia, China. *BMC Gastroenterol* 2016; 16: 2.
13. Zeng Z, Zhu Z, Yang Y, *et al.* Incidence and clinical characteristics of inflammatory bowel disease in a developed region of Guangdong Province, China: a prospective population-based study. *J Gastroenterol Hepatol* 2013; 28: 1148–1153.
14. Chow DK, Leong RW, Tsoi KK, *et al.* Long-term follow-up of ulcerative colitis in the Chinese population. *Am J Gastroenterol* 2009; 104: 647–654.
15. Wan J, Wang X and Zhang Y, *et al.* 5-Aminosalicylic acid prevents disease behavior progression and intestinal resection in colonic and ileocolonic Crohn's disease patients: a retrospective study. *Can J Gastroenterol Hepatol* 2021; 2021: 1412663.
16. Gomollon F, Dignass A, Annese V, *et al.* 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: Diagnosis and medical management. *J Crohns Colitis* 2017; 11: 3–25.
17. Magro F, Gionchetti P and Eliakim R, *et al.* Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: Definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. *J Crohns Colitis* 2017; 11: 649–670.
18. von Elm E, Altman DG and Egger M, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370: 1453–1457.

19. Silverberg MS, Satsangi J, Ahmad T, *et al*. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *Can J Gastroenterol* 2005; 19(Suppl. A): 5A–36A.

20. Li X, Wu C, Lu J, *et al*. Cardiovascular risk factors in China: a nationwide population-based cohort study. *Lancet Public Health* 2020; 5: e672–e681.

21. Yang H, Zhou R, Bai X, *et al*. Trend and geographic variation in incidence and prevalence of inflammatory bowel disease in regions across China: a nationwide employee study between 2013 and 2016. *Front Med (Lausanne)* 2022; 9: 900251.

22. Ng WK, Wong SH and Ng SC. Changing epidemiological trends of inflammatory bowel disease in Asia. *Intest Res* 2016; 14: 111–119.

23. Jiang L, Xia B, Li J, *et al*. Retrospective survey of 452 patients with inflammatory bowel disease in Wuhan city, central China. *Inflamm Bowel Dis* 2006; 12: 212–217.

24. Yao LY, Shao BL, Tian F, *et al*. Trends in medication use and treatment patterns in Chinese patients with inflammatory bowel disease. *World J Gastroenterol* 2022; 28: 4102–4119.

25. Yang H, Li Y, Wu W, *et al*. The incidence of inflammatory bowel disease in Northern China: a prospective population-based study. *PLoS One* 2014; 9: e101296.

26. Burisch J, Katsanos KH, Christodoulou DK, *et al*. Natural disease course of ulcerative colitis during the first five years of follow-up in a European population-based inception cohort – an Epi-IBD study. *J Crohns Colitis* 2019; 13: 198–208.

27. Burisch J, Kiudelis G, Kupcinskas L, *et al*. Natural disease course of Crohn's disease during the first 5 years after diagnosis in a European population-based inception cohort: an Epi-IBD study. *Gut* 2019; 68: 423–433.

28. Li Y, Chen B, Gao X, *et al*. Current diagnosis and management of Crohn's disease in China: results from a multicenter prospective disease registry. *BMC Gastroenterol* 2019; 19: 1–14.

29. Jiang XL and Cui HF. An analysis of 10218 ulcerative colitis cases in China. *World J Gastroenterol* 2002; 8: 158–161.

30. Solberg IC, Lygren I, Jahnsen J, *et al*. Clinical course during the first 10 years of ulcerative colitis: results from a population-based inception cohort (IBSEN Study). *Scand J Gastroenterol* 2009; 44: 431–440.

31. Hu D, Ren J, Wang G, *et al*. Geographic mapping of Crohn's disease and its relation to affluence in Jiangsu province, an eastern coastal province of China. *Gastroenterol Res Pract* 2014; 2014: 590467.

32. Ng SC, Tang W, Ching JY, *et al*. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. *Gastroenterology* 2013; 145: 158–165 e2.

33. Torres J, Bonovas S, Doherty G, *et al*. ECCO guidelines on therapeutics in Crohn's disease: medical treatment. *J Crohns Colitis* 2020; 14: 4–22.

34. Arieira C, Curdia Goncaves T, Dias de Castro F, *et al*. Clinical course in Crohn's disease: factors associated with behaviour change and surgery. *Scand J Gastroenterol* 2018; 53: 1222–1227.

35. Kerur B, Machan JT, Shapiro JM, *et al*. Biologics delay progression of Crohn's disease, but not early surgery, in children. *Clin Gastroenterol Hepatol* 2018; 16: 1467–1473.

36. Hoie O, Wolters FL, Riis L, *et al*. Low colectomy rates in ulcerative colitis in an unselected European cohort followed for 10 years. *Gastroenterology* 2007; 132: 507–515.

37. Gionchetti P, Dignass A, Danese S, *et al*. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 2: Surgical management and special situations. *J Crohns Colitis* 2017; 11: 135–149.

38. Chen M, Yi F, Zhou F, *et al*. Risk factors for initial surgery in patients with Crohn's disease in Central China. *Surg Today* 2015; 45: 1002–1008.