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REVIEW ARTICLE

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Current status of IBD and surgery of Crohn's disease in Thailand

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Abstract

Inflammatory bowel disease (IBD) consists of two diseases: ulcerative colitis (UC) and Crohn's disease (CD). The incidence of IBD is much higher in Western countries compared to Asian countries, especially in Thailand. The incidence of UC in Thailand is quite low and seems less aggressive than in Western countries. Over the past two decades, the evolution of UC management in Thailand has led to a reduction in hospitalization and colectomy rate. Regarding CD, the majority of patients have an inflammatory phenotype at diagnosis. Diagnosis of CD remains challenging in Thailand as the time from onset of symptoms to diagnosis is quite delayed, possibly due to unawareness and difficulty in the differential diagnosis between CD and other infectious entero-colitis such as intestinal tuberculosis. With a significant trend to early initiation of immunomodulators and biologics, the cumulative rate of surgery after diagnosis has been improved. To improve the outcomes of CD treatment in Thailand, physicians need more awareness to recognize the disease, which results in early diagnosis, prevention of long-term complications, and reduction in the rate of surgery.

KEYWORDS

Asian, Crohn's disease, inflammatory bowel disease, Thailand, ulcerative colitis

1 | INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory diseases associated with either transmural granulomatous inflammation or inflammation limited to mucosa and submucosa. It is believed that they are caused by an immune response in a genetic predisposition in an antigenic stimulation of the gut microbiota.[1] Comparing to the Western population, the incidence of IBD is lower in Asia. Due to physician awareness, better access to health care, and diagnostic facilities, the increasing prevalence was recently reported from population-based and referral center studies.[2-4] The growing inclination for IBD, which exceeded the non-immigrants, also appeared in Asians who migrated to Western countries.[5-7] This seems to support that environmental factors contribute to a critical role in disease development.

Crohn's disease is less common in Asia when compared to UC. Meanwhile, the preliminary data suggested that the incidence of CD might overtake the incidence of UC over time in developed Western countries.[8-12] Because the prevalence of these two diseases is low and most publications were reported from hospital-based cohort studies and population-based results from Korea and Japan, the management of IBD in Asia has been quite different, county to country.[13-17]

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In Thailand, the prevalence and incidence of IBD are quite low comparing to both Western and other Asia-Pacific countries. In the past, only small sample size IBD cohorts without prospective longitudinal clinical data were reported in Thailand.[18] Moreover, the incidence of IBD is also lower comparing to other major colorectal diseases in Thai patients. Of these, colorectal cancer seems to be the most common disease and it has been increasingly performed with minimally invasive surgery mostly in high-volume university hospitals by board-certified colorectal surgeons or well-trained laparoscopic surgeons.[19] Therefore, we summarized the current status of IBD and surgery of Crohn's disease in Thailand, including patient characteristics and disease management based on two recent retrospective longitudinal studies regarding CD and UC, which were published from the collaboration between the two largest university hospitals in Bangkok, Thailand: the Faculty of Medicine Siriraj Hospital, Mahidol University, and King Chulalongkorn Memorial Hospital.

2 | ULCERATIVE COLITIS

Ulcerative colitis (UC) is a chronic relapsing disease that normally develops at an early age and persists throughout life. It disturbs the patient's quality of life and differs in varying populations and regions. High prevalence in Western countries such as North America and Europe was reported, but the low prevalence in Asia was also noticed. Several studies from the high-prevalence area reported that approximately 50% of patients with UC need corticosteroids at 10 years. The UC-related colectomy rate at 10 years is around 10% to 15%, while the UC-related hospitalization rate at 10 years is nearly half.[20] However, long-term study from low-incidence countries is lacking. In the Asia-Pacific, Thailand has the lowest incidence of UC with an incidence of 0.2 per 100,000 population.[21] Hence, we updated the data from a recent retrospective study published from the collaboration between the two largest university hospitals in Thailand, which represents a low-incidence area regarding the disease course, including the rates of endoscopic healing, hospitalization, and colectomy. The study included 291 UC patients followed in two separate cohorts between 2000 and 2018; 119 patients between 2000 and 2009 comprised the early cohort and the other 172 patients between 2010 and 2018 comprised the later cohort. The median follow-up in both cohorts was 10 and 4 years, respectively.[22]

2.1 | Clinical characteristics of UC patients

There was no difference in all patient characteristics between the two cohorts. The median age was approximately 42 years in both UC cohorts. There was no difference between genders (53% female). According to smoking, most patients were non-smokers (90%), 9% were former smokers, and only 1% were active smokers. Approximately 5% of patients in both cohorts underwent appendectomy. Interestingly, none of them had a family history of inflammatory bowel disease, which was different from the Western countries. During the study period, there was no difference in either UC location at diagnosis or extraintestinal manifestation (10%) between the two cohorts.

2.2 | Medical treatment in UC patients

Comparing the two cohorts, there was no difference in utilization of systemic steroids. In contrast, the utilization of combination treatment of oral and topical Mesalamine in the later cohort was significantly increased compared to the early cohort. For Thiopurine utilization, a significant increase in the utilization of Thiopurine between the two cohorts was observed. The median duration from diagnosis to Thiopurine initiation in the early cohort was significantly longer than the later cohort. Comparing the early and the later cohorts, the cumulative probability of receiving Thiopurine was 21% vs 29% at 1 year, 35% vs 49% at 3 years, and 42% vs 63% at 5 years after diagnosis. Only three patients in the early cohort and one patient in the later cohort required biological agents. The cumulative probability of receiving biological agents was 1% at 5 years after diagnosis in both cohorts.

2.3 | Endoscopic healing

There was a significant increase in the mucosal healing rate in the later cohort. Comparing the early and later cohorts, the cumulative probability of achieving mucosal healing was 8% vs 16% at 1 year, 15% vs 46% at 2 years, and 27% vs 58% at 5 years after diagnosis. A decreased risk of achieving endoscopic healing was observed in patients under 40 years of age at diagnosis and UC patients diagnosed in the early cohort.

2.4 | UC-related hospitalization

Approximately one-fifth of patients required at least one hospitalization at some point during the disease course. There was a significant decrease in the rate of UC-related hospitalization in the later cohorts when compared with those in the early cohort. The cumulative probability of requiring UC-related hospitalization was 80% vs 5% at 1 year, 28% vs 12% at 2 years, and 30% vs 21% at 5 years in the early and later cohorts, respectively. Factors associated with UC-related hospitalization were extensive colitis and UC patients in the early cohort.

2.5 | UC-related colectomy

Approximately 5% of UC patients from both cohorts underwent colectomy during follow-up. The indications for surgery were a medical failure, superimposed severe cytomegalovirus

(CMV)-related colitis, and high-grade dysplasia. The rate of colectomy in the later cohort significantly decreased when compared with the early cohort, as demonstrated by the cumulative probability of colectomy at 5 years after diagnosis: 6% in the early cohort vs 2% in the later cohort. Although there was no statistical significance, the risk of colectomy was also detected in patients with extensive colitis with a hazard ratio of 1.9 and UC patients in the early cohort with a hazard ratio of 2.8. The prevalence of UC surgery decreased over the period of the study, which was quite similar to two recently published Japanese studies: one nationwide cohort study and a questionnaire survey study of surgical institutions in Japan. Both studies from Japan demonstrated that the prevalence of UC-related surgery seems to be decreasing according to the increasing rate of anti-tumor necrosis factor (TNF) agent and calcineurin inhibitors administration. However, the prevalence of urgent or emergent surgery remains unchanged. Interestingly, the most distinctive change in surgical indications in one of those studies was the increase in cancer or dysplasia from 20.2% in 2007 to 34.8% in 2017.[23, 24]

2.6 | UC-related cancer and death

Regarding UC-related colorectal cancer and death, none of the patients had colorectal cancer. One patient maintaining with Thiopurine in the early cohort died from severe bacterial pneumonia. No death occurred in the later cohort.

3 | CROHN'S DISEASE

The prevalence of Crohn's disease is increasing in the Asian population. Although some long-term Crohn's disease cohorts from Asia have been reported, most of them from East and South Asia.[25] Data from Southeast Asia, particularly from Thailand, remains limited, with only a few reports available on the topic in the literature. We reviewed and discussed a study that included all adult patients over 18 years of age treated and diagnosed with CD between 2000 and 2017 at Siriraj Hospital and King Chulalongkorn Memorial Hospital.[26] CD was diagnosed based on clinical, endoscopic, and pathologic findings, and the diagnosis was confirmed by clinical and/or endoscopic response to Crohn's disease treatment. The remaining 182 patients after excluding patients followed up less than 6 months were included in this study. The median follow-up time was 4.6 years. The patients were divided into the early or the late cohort similar to the aforementioned UC study.

3.1 | Clinical characteristics of CD patients

The mean age of patients was 46 years; half of them were male patients. Ninety percent of patients had never smoked, and only 5% were current smokers. There was no significant difference in other demographic data between the two cohorts. At diagnosis, the phenotypic location was 34%, 26%, and 38% for ileal, colonic, and ileocolonic, respectively. Upper gastrointestinal involvement was found in 14% of patients. For disease behavior, 80% of patients had inflammatory, 12% had stricture, and 11% had penetrating phenotype. Perianal disease, including perianal fistula and abscess, was found in 12%. The median duration of presenting symptoms before diagnosis was 12 months. Approximately half of the patients required a single colonoscopy for diagnosis. Thirty-one percent required two colonoscopies, and 17% required more than two colonoscopies. Eleven percent of patients were treated with anti-tuberculosis medications before Crohn's disease was diagnosed. Six percent of patients were diagnosed with CD at the time of surgery. Meanwhile, another 13% of patients had undergone a bowel resection without recognition of Crohn's disease, but it was diagnosed later when the disease was recurrent. In total, nearly one-fifth of patients had been operated on before a definite diagnosis of Crohn's disease was made.

Regarding clinical manifestation, the most common symptom was abdominal pain (76%). Other common symptoms included diarrhea and weight loss. Bleeding per rectum and fever were found in about one-third of patients. Extraintestinal manifestations were observed in 11.5%. There was no significant difference regarding disease phenotypes or clinical presentation between the two cohorts.

3.2 | Medical treatment in CD patients

During follow-up, approximately 75% of patients were prescribed 5-Aminosalicylic acid (5-ASA) and 81% of the patients were prescribed systemic corticosteroids, which was not significantly different between the two cohorts. 84% of the patients received Thiopurine with no significant difference between the two groups. However, the time to start Thiopurine was significantly shorter, and the cumulative exposure to Thiopurine at 1 year and 5 years was significantly longer in the later cohort.

Biologic agents were used in 13% of the patients, with no significant difference between the two groups. Nearly all patients received Infliximab. Only one patient received Adalimumab. Similar to Thiopurine utilization, the patients in the later cohort tended to start biologic agents earlier. The median time to start a biologic agent was 9.3 months in the later cohort and 66 months in the early cohort. The cumulative exposure to biologic agents at 1 year and 5 years was significantly longer in the later cohort.

3.3 | Progression of disease behavior

During follow-up, nearly 10% with inflammatory phenotype at diagnosis developed either bowel stricture or penetration, but there was no difference between the two cohorts. The cumulative rates of behavior change to complicated behavior at 1 year and 5 years were 0% and 10% in the early cohort and 2% and 5.8% in the later cohort, respectively.

3.4 | CD-related hospitalization

Approximately 23% of patients required at least one hospitalization. There was an inclination toward a lower number of patients requiring at least one hospitalization in the later cohort, but the difference between the groups did not achieve statistical significance. The cumulative rates of the first hospitalization at 1 year and 5 years were 13% and 30% in the early cohort and 7.9% and 18% in the later cohort, respectively.

3.5 | CD-related surgery or intervention

During follow-up, approximately one-third of patients required at least one intestinal surgery or intervention. As mentioned, 13% of patients had undergone surgery before the diagnosis of CD was made, and 6% of patients underwent surgery at the time of diagnosis. The types of surgery or intervention were described in Table 1. The cumulative rates of surgery at 1 year and 5 years were 27% and 36% in the early cohort, while they were 24% and 27%, respectively, in the later cohort. After excluding the surgeries before and at diagnosis, the cumulative rate of bowel resection surgery after Crohn's disease diagnosis at 1 and 5 years were 5.5% and 13%, respectively. A significant difference between the two cohorts was not observed which was different from a retrospective multicenter study from Japan, which reported a decreased CD-related surgery trend during the advent of biologic agents.[27] Most CD-related surgeries in Thailand were performed by open surgery, while the minimally invasive surgical approach is more common in other East Asian countries, for instance, Japan. If the expertise is available, a minimally invasive surgical approach to Crohn's disease surgery should typically be considered as recommended by both the American Society of Colon and Rectal Surgeons and the European Crohn's Colitis Organization guidelines. Compared to open surgery, patients with CD undergoing elective laparoscopic surgery demonstrated a shorter length of hospital stay, fewer complications, fewer incisional hernia, and improved pulmonary function. In recurrent CD, A laparoscopic resection is feasible and safe in the presence of appropriate expertise. Although complications do not increase, conversion to open surgery was 2.5 times more frequent in recurrent cases.[28, 29]

TABLE 1 Types of Crohn's disease-related surgery or intervention

Procedures	Number of patients
Ileo-colectomy	6
Right hemicolectomy	21
Left colectomy/sigmoid resection	2
Total colectomy	4
Colectomy (unspecified)	5
Ileal/small bowel resection	9
Loop colostomy/ileostomy	6
Lysis adhesion	2
Percutaneous catheter drainage	2
Gastric ulcer suture	1

3.6 | Factors associated with CD-related surgery or intervention

Multivariate analysis for factors that predict CD-related intestinal surgery after adjusting for age, gender, disease location, disease behavior, perianal involvement, history of previous surgery, use of the biologic agent, and follow-up time demonstrated that the early utilization of Thiopurine was an independent protective factor against surgery with a hazard ratio of 0.3, while upper GI tract involvement was identified as an independent predictor of CD-related intestinal surgery with a hazard ratio of 3.3. In the aforementioned multicenter Japanese study, Shinagawa et al also reported that preoperative smoking (HR,1.40; 95% CI, 1.18-1.68), perianal disease (HR, 1.50; 95% CI, 1.27-1.77), and ileocolic type of CD (HR, 1.42; 95% CI, 1.20-1.69) were significant risk factors for reoperation, while postoperative use of immunomodulators (HR, 0.60; 95% CI, 0.44-0.81) and anti-TNF therapy (HR, 0.71; 95% CI, 0.57-0.88) significantly reduced the risk of CD-related reoperation.[27] Recently, an intensive literature review reported the environmental factors for IBD. It reported that smoking increases the risk of developing CD among current smokers (HR =1.90 [95%CI: 1.42-2.53]). The increased risk is associated with the number of packs per year smoked ($P < 0.0001$), whereas smoking cessation is associated with a reduction in the risk (HR =1.35 [95% CI: 1.05-1.73]). Passive smoking exposure in childhood is no longer considered a risk factor for incident CD. Smoking also increases the risk for advanced and difficult-to-treat disease. It increases the risk of penetrating intestinal complications, strictures or fistulae, and the need for surgical resections (first or second surgery). Smoking cessation results in decreased risk of CD, decreased risk of flares, decreased need for steroids, and immunosuppressive therapy. Current smoking is associated with higher relapse rates. Smoking cessation is associated with a 32% reduction in the risk of a relapse as compared with continued smokers.[30]

3.7 | CD-related cancer

None of the patients diagnosed with CD developed cancer. This possibly due to the short follow-up time of the cohort compared to other cohorts from Asian countries. Mizushima et al published a study regarding the incidence and clinical characteristics of CD-related malignancy in Japan. They reported that the risk of all site cancers was significantly increased from that of the background population; the standardized incidence ratio (SIR) was 2.24 (95% CI 1.19-3.83). Particularly, the risk of colorectal cancer significantly increased in comparison to that of the background population: SIR 5.80 (95% CI 2.13-12.68).[31]

4 | IBD SPECIALIZED PHYSICIANS AND TREATMENT SITUATION IN THAILAND

In Thailand, there are limited numbers of physicians focusing mainly on IBD because IBD was rare in the past. Currently, less than 10 gastroenterologists specialize in IBD, and there are only two special IBD clinics in our country; both are in Bangkok. However, because the incidence is increasing, there are more doctors interested in IBD and more special IBD clinics are going to be established soon, especially in other parts of Thailand. Besides colorectal surgeons and gastroenterologists, IBD needs more other specialists including pathologists, radiologists, nutritionists, and psychiatrists in caring for patients; specialists in these areas are also limited in numbers. Furthermore, medical treatment in Thailand is also quite restricted. The main medical treatment is conventional medications such as 5-ASA, systemic corticosteroids, and immunomodulators especially Azathioprine. The biologic agent is not widely available. In the past, only Infliximab was available, and it has only been in recent years that other biologic agents such as Vedolizumab and Ustekinumab have become available. All biologic agents are not reimbursable by the Thai government; only a few patients can afford them. Therefore, surgery is still the necessary treatment in Thailand.

5 | CONCLUSION

Compared to the West, the natural course of ulcerative colitis in Thailand is less aggressive in terms of the rates of systemic corticosteroid utilization, biologic utilization, UC-related colectomy, and hospitalization. Over the past two decades, the rates of UC-related hospitalization and colectomy in Thailand have been decreasing, which is similar to Western countries.

Similar to UC, the natural history of Crohn's disease in Thailand seems less aggressive than in Western countries. Early disease recognition and early initiation of immunomodulators in CD could help to prevent long-term complications and reduce unnecessary surgery.

There is an interesting question regarding why the prevalence of ulcerative colitis and Crohn's disease in Thailand is lower and the disease activity is less severe than in Western countries. The possible answer to this question is possibly the difference in the genetic and environmental factors. The lower incidence and less aggressive disease activity might have resulted in the difference in ethnicities, which is a genetic factor. Although there has not been a study of genetic factors in Thai IBD patients, differences in the IBD susceptibility genes between Asia and the Western countries have recently been reported.[32] Nucleotide oligomerization domain (NOD)-2 variants associated with CD patients in the West have not been identified in CD in the Han Chinese, Japanese, Korean, Indian, and Malaysian populations.[33-40] Meanwhile, many environmental factors possibly explain the lower severity of disease activity, including the higher incidence of tropical infections such as tuberculosis or diarrhea, the difference in bacterial flora, which is probably caused by the difference in food ingestion and sanitation, and the fact that there are fewer smokers in Thailand, as demonstrated in the two aforementioned studies. Recent data suggested that environmental risk factors in the development of UC may act more rapidly and/or differently to that of CD. The pivotal role of early life events in the development of IBD has been demonstrated in studies from the West, reporting an increased risk of IBD associated with bacterial gastroenteritis and use of antibiotics in the first year of life.[41-43] Epidemiological studies of IBD in Asia have been limited by a lack of patient and physician awareness of these diseases; limited access to medical facilities; difficulty in making a firm diagnosis where other diseases that mimic IBD predominate such as tuberculosis and infectious diarrhea; and difficulty collecting population-based data.[44]

In summary, the prevalence of inflammatory bowel disease, including both ulcerative colitis and Crohn's disease, is low in Thailand. Less severe disease and aggressiveness, lower hospital admission, and lower surgery rate are also observed in Thai IBD patients compared to in Western and other Asian patients. Early recognition of the disease, as well as early initiation of immunomodulators, could decrease the complications and unnecessary operation for Crohn's disease. Ultimately, awareness of the disease by Thai physicians and pathologists might improve the detection rate of this problem in the future.

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REFERENCES

1. Danese S, Fiocchi C. Etiopathogenesis of inflammatory bowel diseases. World J Gastroenterol. 2006;12(30):4807–12.
2. Thia KT, Loftus EV Jr, Sandborn WJ, Yang SK. An update on the epidemiology of inflammatory bowel disease in Asia. Am J Gastroenterol. 2008;103(12):3167–82.
3. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology. 2004;126(6):1504–17.
4. Hou JK, El-Serag H, Thirumurthi S. Distribution and manifestations of inflammatory bowel disease in Asians, Hispanics, and African Americans: a systematic review. Am J Gastroenterol. 2009;104(8):2100–9.
5. Jayanthi V, Probert CS, Pinder D, Wicks AC, Mayberry JF. Epidemiology of Crohn's disease in Indian migrants and the indigenous population in Leicestershire. Q J Med. 1992; 82(298):125–38.
6. Probert CS, Jayanthi V, Pinder D, Wicks AC, Mayberry JF. Epidemiological study of ulcerative proctocolitis in Indian migrants and the indigenous population of Leicestershire. Gut. 1992;33(5):687–93.

7. Probert CS, Jayanthi V, Hughes AO, Thompson JR, Wicks AC, Mayberry JF. Prevalence and family risk of ulcerative colitis and Crohn's disease: an epidemiological study among Europeans and south Asians in Leicestershire. Gut. 1993;34(11):1547–51.
8. Wilson J, Hair C, Knight R, Catto-Smith A, Bell S, Kamm M, et al. High incidence of inflammatory bowel disease in Australia: a prospective population-based Australian incidence study. Inflamm Bowel Dis. 2010;16(9):1550–6.
9. Molinié F, Gower-Rousseau C, Yzet T, Merle V, Grandbastien B, Marti R, et al. Opposite evolution in incidence of Crohn's disease and ulcerative colitis in Northern France (1988–1999). Gut. 2004;53(6):843–8.
10. Bernstein CN, Wajda A, Svenson LW, MacKenzie A, Koehoorn M, Jackson M, et al. The epidemiology of inflammatory bowel disease in Canada: a population-based study. Am J Gastroenterol. 2006;101(7):1559–68.
11. Gearry RB, Richardson A, Frampton CM, Collett JA, Burt MJ, Chapman BA, et al. High incidence of Crohn's disease in Canterbury, New Zealand: results of an epidemiologic study. Inflamm Bowel Dis. 2006;12(10):936–43.
12. Kappelman MD, Rifas-Shiman SL, Kleinman K, Ollendorf D, Bousvaros A, Grand RJ, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. Clin Gastroenterol Hepatol. 2007;5(12):1424–9.
13. Yao T, Matsui T, Hiwatashi N. Crohn's disease in Japan: diagnostic criteria and epidemiology. Dis Colon Rectum. 2000; 43(10):S85–93.
14. Yang SK, Yun S, Kim JH, Park JY, Kim HY, Kim Y-H, et al. Epidemiology of inflammatory bowel disease in the Songpa-Kangdong district, Seoul, Korea, 1986–2005: a KASID study. Inflamm Bowel Dis. 2008;14(4):542–9.
15. Higashi A, Watanabe Y, Ozasa K, Hayashi K, Aoike A, Kawai K. Prevalence and mortality of ulcerative colitis and Crohn's disease in Japan. Gastroenterol Jpn. 1988;23(5):521–6.
16. Sung JJ, Kamm MA, Marteau P. Asian perspectives in the management of inflammatory bowel disease: findings from a recent survey. J Gastroenterol Hepatol. 2010;25(1):183–93.
17. Asakura K, Nishiwaki Y, Inoue N, Hibi T, Watanabe M, Takebayashi T. Prevalence of ulcerative colitis and Crohn's disease in Japan. J Gastroenterol. 2009;44(7):659–65.
18. Pongprasobchai S, Manatsathit S, Leelakusolvong S, Sattawatthamrong Y, Boonyapisit S. Ulcerative colitis in Thailand: a clinical study and long-term follow-up. J Med Assoc Thai. 2001;84(9):1281–8.
19. Lohsiriwat V, Chaisomboon N, Pattana-Arun J. Current Colorectal Cancer in Thailand. Ann Coloproctol. 2020;36(2):78–82.
20. Fumery M, Singh S, Dulai PS, Gower-Rousseau C, Peyrin-Biroulet L, Sandborn WJ. Natural history of adult ulcerative colitis in population-based cohorts: a systematic review. Clin Gastroenterol Hepatol. 2018;16(3):343–56.
21. Ng SC, Tang W, Ching JY, Wong M, Chow CM, Hui AJ, 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(1):158–65.
22. Aniwan S, Limsrivilai J, Pongprasobchai S, Pausawasdi N, Prueksapanich P, Kongtub N, et al. Temporal trend in the natural history of ulcerative colitis in a country with a low incidence of ulcerative colitis from 2000 through 2018. Intestinal Res. 2021;19(2):186–193.
23. Uchino M, Ikeuchi H, Hata K, Okada S, Ishihara S, Morimoto K, et al. Changes in the rate of and trends in colectomy for ulcerative colitis during the era of biologics and calcineurin inhibitors based on a Japanese nationwide cohort study. Surg Today. 2019;49(12):1066–73.
24. Kimura H, Takahashi K, Futami K, Ikeuchi H, Tatsumi K, Watanabe K, et al. Has widespread use of biologic and immunosuppressant therapy for ulcerative colitis affected surgical trends? Results of a questionnaire survey of surgical institutions in Japan. Surg Today. 2016;46(8):930–8.
25. Ye BD, Yang SK, Cho YK, Park SH, Yang D-H, Yoon SM, et al. Clinical features and long-term prognosis of Crohn's disease in Korea. Scand J Gastroenterol. 2010;45(10):1178–85.
26. Limsrivilai J, Aniwan S, Sudcharoen A, et al. Temporal trend of disease recognition, treatment paradigm, and clinical outcomes of Crohn disease in Thailand from 2000 through 2017: Is early use of thiopurines beneficial? Medicine (Baltimore). 2020;99(38):e22216.
27. Shinagawa T, Hata K, Ikeuchi H, Fukushima K, Futami K, Sugita A, et al. Rate of reoperation decreased significantly after year 2002 in patients with Crohn's disease. Clin Gastroenterol Hepatol. 2020;18(4):898–907.
28. Lightner AL, Vogel JD, Carmichael JC, Keller DS, Shah SA, Mahadevan U, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical Management of Crohn's Disease. Dis Colon Rectum. 2020;63(8):1028–52.
29. Adamina M, Bonovas S, Raine T, Spinelli A, Warusavitarne J, Armuzzi A, et al. ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Treatment. J Crohns Colitis. 2020;14(2):155–68.
30. Abegunde AT, Muhammad BH, Bhatti O, Ali T. Environmental risk factors for inflammatory bowel diseases: Evidence based literature review. World J Gastroenterol. 2016;22(27):6296–317.
31. Mizushima T, Ohno Y, Nakajima K, Kai Y, Iijima H, Sekimoto M, et al. Malignancy in Crohn's disease: incidence and clinical characteristics in Japan. Digestion. 2010;81(4):265–70.
32. Ng SC, Tsoi KK, Kamm MA, Xia B, Wu J, Chan FKL, et al. Genetics of inflammatory bowel disease in Asia: systematic review and meta-analysis. Inflamm Bowel Dis. 2012;18(6):1164–76.
33. Leong RW, Armuzzi A, Ahmad T, Wong ML, Tse P, Jewell DP, et al. NOD2/CARD15 gene polymorphisms and Crohn's disease in the Chinese population. Aliment Pharmacol Ther. 2003;17 (12):1465–70.
34. Guo QS, Xia B, Jiang Y, Qu Y, Li J. NOD2 3020insC frameshift mutation is not associated with inflammatory bowel disease in Chinese patients of Han nationality. World J Gastroenterol. 2004;10(7):1069–71.
35. Li M, Gao X, Guo CC, Wu KC, Zhang X, Hu PJ. OCTN and CARD15 gene polymorphism in Chinese patients with inflammatory bowel disease. World J Gastroenterol. 2008;4(31):4923–7.
36. Yamazaki K, Takazoe M, Tanaka T, Kazumori T, Nakamura Y. Absence of mutation in the NOD2/CARD15 gene among 483 Japanese patients with Crohn's disease. J Hum Genet. 2002;47(9):469–72.
37. Inoue N, Tamura K, Kinouchi Y, Fukuda Y, Takahashi S, Ogura Y, et al. Lack of common NOD2 variants in Japanese patients with Crohn's disease. Gastroenterology. 2002;123(1):86–91.
38. Croucher PJ, Mascheretti S, Hampe J, Huse K, Frenzel H, Stoll M, et al. Haplotype structure and association to Crohn's disease of CARD15 mutations in two ethnically divergent populations. Eur J Hum Genet. 2003;11(1):6–16.
39. Pugazhendhi S, Amte A, Balamurugan R, Subramanian V, Ramakrishna BS. Common NOD2 mutations are absent in patients with Crohn's disease in India. Indian J Gastroenterol. 2008;27(5):201–3.
40. Chua KH, Hilmi I, Ng CC, Eng TL, Palaniappan S, Lee WS, et al. Identification of NOD2/CARD15 mutations in Malaysian patients with Crohn's disease. J Dig Dis. 2009;10(2):124–30.
41. Gradel KO, Nielsen HL, Schønheyder HC, Ejlertsen T, Kristensen B, Nielsen H. Increased short- and long-term risk of inflammatory bowel disease after salmonella or campylobacter gastroenteritis. Gastroenterology. 2009;137(2):495–501.

42. García Rodríguez LA, Ruigómez A, Panés J. Acute gastroenteritis is followed by an increased risk of inflammatory bowel disease. Gastroenterology. 2006;130(6):1588–94.
43. Shaw SY, Blanchard JF, Bernstein CN. Association between the use of antibiotics in the first year of life and pediatric inflammatory bowel disease. Am J Gastroenterol. 2010;105(12):2687–92.
44. Prideaux L, Kamm MA, De Cruz PP, Chan FK, Ng SC. Inflammatory bowel disease in Asia: a systematic review. J Gastroenterol Hepatol. 2012;27(8):1266–80.

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