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Epidemiology and Natural History of Elderly-onset Inflammatory Bowel Disease: Results From a Territory-wide Hong Kong IBD Registry

Joyce Wing Yan Mak,[a] Carmen Lok Tung Ho,[b] Kylie Wong,[a] Tsz Yan Cheng,[a] Terry Cheuk Fung Yip,[a] Wai Keung Leung,[c] Michael Li,[d] Fu Hang Lo,[e] Ka Man Ng,[f] Shun Fung Sze,[g] Chi Man Leung,[h] Steven Woon Choy Tsang,[i] Edwin Hok Shing Shan,[j] Kam Hon Chan,[k] Belsy C. Y. Lam,[l] Aric Josun Hui,[m] Wai Hung Chow,[n] Siew Chien Ng[a]

[a]Department of Medicine and Therapeutics, Institute of Digestive Disease, Chinese University of Hong Kong, Hong Kong [b]Imperial College School of Medicine, London, UK [c]Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong [d]Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong [e]Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong [f]Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong [g]Department of Medicine, Queen Elizabeth Hospital, Hong Kong [h]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong [i]Department of Medicine, Tseung Kwan O Hospital, Hong Kong [j]Department of Medicine and Geriatrics, Caritas Medical Centre, Hong Kong [k]Department of Medicine, North District Hospital, Hong Kong [l]Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong [m]Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong [n]Department of Medicine, Yan Chai Hospital, Hong Kong

Corresponding author: Siew C. Ng, MBBS (Lond), PhD (Lond), FRCP (Lond), FRCP (Edin), AGAF, FHKCP, FHKAM (Med), Institute of Digestive Disease, Department of Medicine and Therapeutics, State Key Laboratory of Digestive Disease, Chinese University of Hong Kong, Hong Kong. Tel.: +852 3505 3996; fax:+852 2637 3852; email: siewchienng@cuhk.edu.hk

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Abstract

Background: Elderly-onset inflammatory bowel disease [IBD], defined as age ≥60 at diagnosis, is increasing worldwide. We aimed to compare clinical characteristics and natural history of elderly-onset IBD patients with those of adult-onset IBD patients.

Methods: Patients with a confirmed diagnosis of IBD from 1981 to 2016 were identified from a territory-wide Hong Kong IBD registry involving 13 hospitals. Demographics, comorbidities, clinical features, and outcomes of elderly-onset IBD patients were compared with those of adult-onset IBD patients.

Results: A total of 2413 patients were identified, of whom 270 [11.2%] had elderly-onset IBD. Median follow-up duration was 111 months (interquartile range [IQR]: 68–165 months). Ratio of ulcerative colitis [UC]: Crohn's disease [CD] was higher in elderly-onset IBD than in adult-onset IBD patients [3.82:1 vs 1.39:1; p <0.001]. Elderly-onset CD had less perianal involvement [5.4% vs 25.4%; p <0.001] than adult-onset CD. Elderly-onset IBD patients had significantly lower cumulative use of immunomodulators [p = 0.001] and biologics [p = 0.04]. Elderly-onset IBD was associated with higher risks of: cytomegalovirus colitis (odds ratio [OR]: 3.07; 95% confidence interval [CI] 1.92–4.89; p <0.001); herpes zoster [OR: 2.42; 95% CI 1.22–4.80; p = 0.12]; and all cancer development [hazard

ratio: 2.97; 95% CI 1.84–4.79; p <0.001]. They also had increased number of overall hospitalisations [OR: 1.14; 95% CI 1.09–1.20; p <0.001], infections-related hospitalisation [OR: 1.87; 95% CI 1.47–2.38; p <0.001], and IBD-related hospitalisation [OR: 1.09; 95% CI 1.04- 1.15; p = 0.001] compared with adult-onset IBD patients.

Conclusions: Elderly-onset IBD was associated with increased risk of infections and cancer development, and increased infection- and IBD-related hospitalisations. Specific therapeutic strategies to target this special population are needed.

Key Words: Elderly-onset IBD; epidemiology; clinical outcomes

1. Introduction

The incidence of inflammatory bowel disease [IBD] is increasing globally. There has been a worldwide accelerating rise in the incidence of IBD in all age groups.[1,2] Rising incidence is reported in newly industrialised countries that were once considered low-prevalence regions, such as Asia, as a consequence of Westernised lifestyles and diets.[3] This epidemiological change, together with the ageing population, has led to the rapid increase in numbers of elderly patients with IBD. A recent systematic review showed that on average, one in 8600 older adults aged >60 years were diagnosed annually with ulcerative colitis [UC], and one in 22 000 were diagnosed with Crohn's disease [CD] in the Western world. [4] It is predicted that the prevalence of IBD among the elderly in Canada will be 1370 per 100 000 population in year 2030, causing a significant burden to the health care system.[5]

Traditionally, IBD is a disease of young adults with the peak incidence between the ages of 20 to 39.[6] However, around one-third of the IBD population are 60 years or older, of whom up to 15% were diagnosed after the age of60 years.[7] Data on the elderly with IBD are difficult to extract as this group of patients is usually excluded from clinical trials. Elderly patients typically have multiple comorbidities and polypharmacy, making disease diagnosis and management more challenging when compared with younger adults. A previous population-based study in elderly-onset IBD in France showed that elderly-onset IBD patients had a milder clinical course.[8] A recent systematic review has shown that elderly IBD patients had less complicated disease and use of immunomodulators, but they had similar or even higher rates of surgery than non-elderly IBD patients. Whether this reflected a true relatively benign course of IBD, or physicians' reluctance to start immunomodulators in the elderly, or both, remained uncertain.[7] Previous systematic reviews only included data from the Western countries or included data from single centre only.[9,10] Limited population-based data on the epidemiology and outcomes are available in Asian elderly-onset IBD patients.[11–14] Our previous study on elderly-onset UC in Hong Kong showed that elderly-onset UC patients had higher all-cause mortality [7.0% vs 1.0%; p <0.001] and UC-related mortality [1.9% vs 0.2%; p = 0.017] compared with non-elderly onset UC patients. Elderly-onset was an independent risk factor for cytomegalovirus infection.[15] Thus, we aimed to investigate the incidence, clinical features, natural history, and outcomes of patients with elderly-onset IBD in Hong Kong, using a territory-wide database, and to directly compare the long-term outcome with that of the corresponding adult-onset IBD patients.

2. Methods

2.1. Materials and subjects

All patients with a confirmed diagnosis of IBD were identified from the Nixon-TAM Hong Kong IBD registry [HKIBDR]. The HKIBDR is a territory-wide cohort developed in 2013, which aims to investigate the prevalence, disease characteristics, treatment, and prognosis of IBD patients in Hong Kong.[16] Thirteen public hospitals under the Hospital Authority across seven clusters in Hong Kong participated in this project; these hospitals serve more than 95% of IBD patients in Hong Kong. The Hong Kong Hospital Authority is the sole public health care provider for primary, secondary, and tertiary health services in Hong Kong, covering 95% of all secondary and tertiary care in Hong Kong with a population of around 7.4 million.[17] Patients in the HKIBD Registry were identified from the Clinical Data Analysis and Reporting System [CDARS] of the Hong Kong Hospital Authority, in which all essential clinical information including: patients' demographics, hospitalisations, visits to outpatient clinics and emergency departments, diagnoses, laboratory results, procedures, prescriptions, dispensing of medications, and deaths are recorded. Patients were identified from CDARS using the following International Classification of Diseases codes [Clinical Modification, Ninth Revision]: 'Regional enteritis' [555.0, 555.1, 555.2, 555.9], 'ulcerative colitis' [556], and 'ulceration of intestine' [569.82], or from individual hospital IBD databases. Duplicated cases were excluded. Various high-quality population-based studies have been published using data from CDARS.[18–21]

We also performed a survey of all the private gastroenterologists in Hong Kong to collect the number of patients with IBD in the private sector, and we estimated that only a small proportion of patients with IBD [<5%] remained under the care of private physicians. The population of Hong Kong is racially and ethnically homogeneous with little migration. The diagnosis of IBD was confirmed from clinical, endoscopic, and radiological findings by clinicians and researchers of each individual institution. A central co-ordinator at the Chinese University of Hong Kong cross-checked the information from each individual institution for case verification. Those with confirmed or suspected intestinal infectious gastroenteritis, tuberculosis, and amoebiasis were excluded. Follow-up review of case notes was performed 6 months later to ensure that the diagnosis remained accurate. Patients were excluded from the analysis if the diagnosis of IBD was not confirmed.

A total of 2413 IBD patients were identified from the Hong Kong IBD registry [HKIBDR]. Detailed electronic medical records of the included patients were reviewed using the Clinical Management System [CMS] of the Hong Kong Hospital Authority, which is a computerised clinical management system recording all key clinical information of each individual patient, including demographic data, inpatient and outpatient consultation notes, diagnoses, drug prescriptions, laboratory results, detailed endoscopic records, and surgical procedures [http://www.ha.org.hk/haconvention/hac2006proceedings/doc/S10_2.pdf].

Electronic patient records in the Hospital Authority are then transferred from the CMS to CDARS for audit and research proposes. We define elderly-onset IBD as those with disease onset at

an age of 60 years or older.[22] Adult-onset IBD was defined as those with disease onset at an age of 18 years or older, but below 60 years. Patients were followed from the date of diagnosis [January 1981] till the end of data collection [30 June 2019], loss to follow-up, or death. Demographic data, including age, gender, smoking history, disease phenotypes [according to the Montreal Classification], and IBD-related medical therapies [including the use of immunosuppressants, 5-aminosalicylates, steroids, and biologics and IBD-related surgeries] were retrieved case by case from CMS. Data after the establishment of HKIBDR were prospectively collected, and those dating from before 2013 were retrospectively retrieved from the CMS. Occurrence of opportunistic infections, including cytomegalovirus [CMV], herpes zoster virus [HZV], *Clostridium difficile* [*C. difficile*], and tuberculosis [TB], and cancer development during follow-up were recorded. CMV infection was defined as positive haematoxylin and eosin stain together with immunohistochemistry, and *C. Difficile* was defined as positive *C. difficile* A&B toxin enzyme immunoassay, or gene polymerase chain reaction [PCR], or culture in stool. HZV infection was defined as positive PCR for the virus in any vesicular fluid samples, and TB was defined as positive culture for *Mycobacterium tuberculosis* [MTB] in any specimen. The numbers of hospitalisations and lengths of stay after IBD diagnosis, as well as mortality, were also recorded.

2.2. Data and statistical analysis

All collected clinical information was entered into a custom-built Microsoft Excel database. The incidence, clinical characteristics, natural history, and medication used were compared between elderly-onset and adult-onset IBD. Age-specific incidence was calculated for adult-onset and elderly-onset IBD, CD, and UC, based on the number of patients diagnosed compared with the total population at risk in each calendar year. Projected population data by age and sex were obtained from the Census and Statistics Department, Hong Kong. Continuous variables were expressed in the mean ± standard deviation or median (interquartile range [IQR]) as appropriate, and categorical variables were presented as the number [percentage]. Qualitative and quantitative differences between subgroups were analysed by chi square or Fisher's exact tests for categorical parameters and Mann-Whitney tests for continuous parameters, as appropriate. Kaplan-Meier analysis was performed to calculate the cumulative probabilities of surgery, cancer, and use of immunomodulators and biologics. Log-rank testing was used to assess for any difference in terms of cumulative probabilities. The age- and sex-standardised incidence ratio for any cancer and the mortality ratio in IBD patients compared with the general population were estimated by Poisson model. Statistical significance was taken as $p < 0.05$. Statistical analysis was performed using Statistical Product and Service Solutions [SPSS] version 25.0 [SPSS, Chicago, IL], and R software [3.6.0; R Foundation for Statistical Computing, Vienna, Austria]. This study was approved by the ethics committee of each individual hospital participating.

3. Results

A total of 2413 patients were identified, of whom 270 [11.2%] had elderly-onset IBD during a median follow-up of 111 months [IQR: 68–165 months]. We studied the yearly incidence of elderly-onset IBD in Hong Kong. The overall incidence of elderly-onset IBD in Hong Kong increased from 0.15 per 100 000 population in years 1986–90 to 1.72 per 100 000 population in years 2011–15. The incidence of elderly-onset UC increased more rapidly compared with that of elderly-onset CD. Incidence of elderly-onset UC was 0.15 per 100 000 population in years 1986–90 and rose to 1.25 per 100 000 population in years 2011–15; there was no case of elderly-onset CD in years 1986–90 but the incidence rose to 0.46 per 100 000 population in years 2011–15. [Figure 1] Compared with adult-onset IBD, the incidences of elderly-onset CD and UC have been increasing from years 1986–90 to years 2011–15; the incidence of adult-onset of CD has been static since year 2001; and that of adult-onset UC has been decreasing since year 2001 [Figure 2].

3.1. Clinical characteristics

There was a male predominance in both elderly-onset [57.8%] and adult-onset IBD [60%] groups. The ratio of UC to CD was higher in elderly-onset IBD than in adult-onset IBD patients [3.82:1 versus. 1.39:1; $p < 0.001$]. Elderly-onset Crohn's disease [CD] had

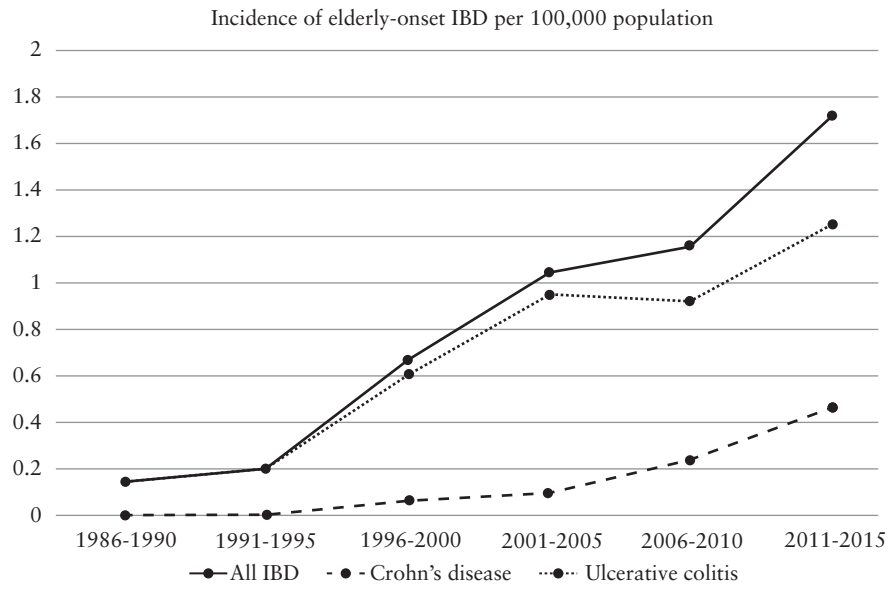


Figure 1. Incidence of elderly-onset inflammatory bowel disease [IBD] in Hong Kong from year 1986 to year 2015.

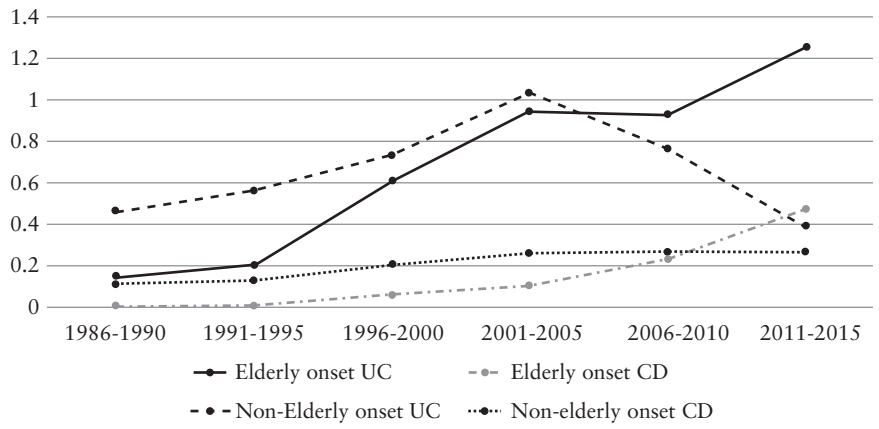


Figure 2. Incidence of elderly-onset inflammatory bowel disease [IBD] and adult-onset IBD in Hong Kong from year 1986 to year 2015.

less perianal involvement [5.4% vs 25.4%; p <0.001] but more stricturing phenotype [32.1% vs 20.5%; p = 0.04] than adult-onset IBD [Table 1]. There was no significant difference in terms of types of medications used [5-aminosalicylates [5-ASA, steroids, immunomodulators, and biologics] at diagnosis of IBD [Table 1]. The majority of the elderly-onset IBD patients [71.2%] were on 5-ASA; 42 [77.8%] elderly-onset CD patients were on 5-ASA at diagnosis. At maximal follow-up, 64.3% [n = 36] of elderly-onset CD patients were on 5-ASA and 48.2% of them had complicated disease phenotype [stricturing/ penetrating behaviour].

3.2. Use of immunomodulators and biologics

There were significantly lower cumulative probabilities of immunomodulator [p <0.001] and biologic use [p = 0.04] in elderly-onset IBD patients compared with adult-onset IBD patients [Figure 3]. The cumulative probabilities of immunomodulator use in elderly-onset IBD were 10.6%, 15.4%, and 20.9% at 1 year, 3 years, and 5 years, respectively, whereas cumulative probabilities of immunomodulator use in adult-onset IBD were 17.6%, 25.4%, and 30% at 1 year, 3 years, and 5 years, respectively. Cumulative probabilities of biologic use in elderly-onset IBD at 1 year, 3 years, and 5 years were 0.4%, 0.8%, and 1.2%, respectively, whereas those in adult-onset IBD at 1 year, 3 years, and 5 years were 1.3%, 2.9%, and 4.4%, respectively.

3.3. IBD-related surgery, cancer risk, and mortality

The cumulative probabilities of having IBD-related surgeries were not significantly different statistically between elderly-onset and adult-onset IBD patients [p = 0.918] [Figure 4]. We performed interaction tests to look at the impact on year of IBD diagnosis and biologic use and requirement of IBD-related surgeries. There was no significant interaction effect between year of IBD diagnosis, biologic use, and IBD-related surgeries [adjusted hazard ratio: 1.17; 95% CI 0.48–2.88; p = 0.73]. However, in terms of all-cancer development, elderly-onset IBD patients were more likely to develop cancers compared with adult-onset IBD after adjusting for genderand smoking and drinking history (hazard ratio [HR]: 1.82; 95% CI 1.16–2.85; p <0.001). Cumulative probabilities of all-cancer development in elderly-onset IBD at 1 year, 3 years, and 5 years were 0.8%, 2.3%, and 4%, respectively, whereas those in adult-onset IBD at 1 year, 3 years, and 5 years were 0.5%, 0.8%, and 1%, respectively. Similarly, elderly-onset IBD was associated with higher all-cause mortality rate compared with adult-onset IBD [HR: 7.92; 95% CI 4.57–13.72; p <0.001].We further looked at the standardised incidence ratio [SIR] of cancer and standardised mortality ratio [SMR] in IBD patients and the general population. The SIR for cancer among IBD patients was 1.04 [95% CI 0.80–1.33], which was not significantly different from the general population after adjusting for age, sex, and calendar year. However, the SMR was lower in the IBD population at 0.57 [95% CI 0.41–0.76] compared with the general population, after adjusting for age, sex, and calendar year.

3.4. Opportunistic infections and hospitalisations

Elderly-onset IBD patients were associated with significantly higher risks of development of cytomegalovirus colitis [CMV] (odds ratio [OR]: 3.07; 95% CI 1.92–4.89; p <0.001] and herpes zoster infections [OR: 2.42; 95% CI 1.22–4.80; p = 0.012] compared with adult-onset IBD. However, there was no statistically significant difference in the risks of tuberculosis [OR: 1.45; 95% CI 0.60–3.50; p = 0.405] and *Clostridium difficile* infection [OR: 0.81; 95% CI 0.29–2.29; p = 0.693] between elderly-onset and adult-onset IBD patients. Elderly-onset IBD had a higher overall number of hospitalisations [OR: 1.14; 95% CI 1.09–1.20; p <0.001], higher number of infections-related [OR: 1.87; 95% CI 1.47–2.38; p <0.001] and IBD-related hospitalisations [OR: 1.09; 95% CI 1.04–1.15; p = 0.001], and longer duration of hospitalisation [OR: 1.004; 95% CI 1.001-1.007; p = 0.007] within the first 2 years of IBD diagnosis compared with adult-onset IBD [Table 2]. We also performed interaction teststo look at the impact of year of IBD diagnosis and biologic use on number of IBD-related hospitalisations. There was no significant interaction effect between year of IBD diagnosis, biologic use, and number of IBD-related hospitalisations [adjusted odds ratio 1.53: 95% CI 0.95–1.18; p = 0.13].

4. Discussion

Our population-based cohort has found a nearly 9-fold increase in the incidence of elderly-onset IBD in Hong Kong from 1986 to 2015. Elderly-onset IBD patients had similar risks of IBD-related surgeries, but increased numbers of opportunistic infections, cancers, and hospitalisations; however, there was significantly less use of immunosuppressants and biologics compared with adult-onset IBD patients. The lower usage of immunosuppressants and biologics in elderly-onset IBD patients could be due to several reasons. These include physicians' misperception of a milder disease course in elderly IBD patients, physicians' familiarity with and safety of corticosteroids,

Table 1. Clinical characteristics of elderly-onset and adult-onset inflammatory bowel disease [IBD] patients in Hong Kong.

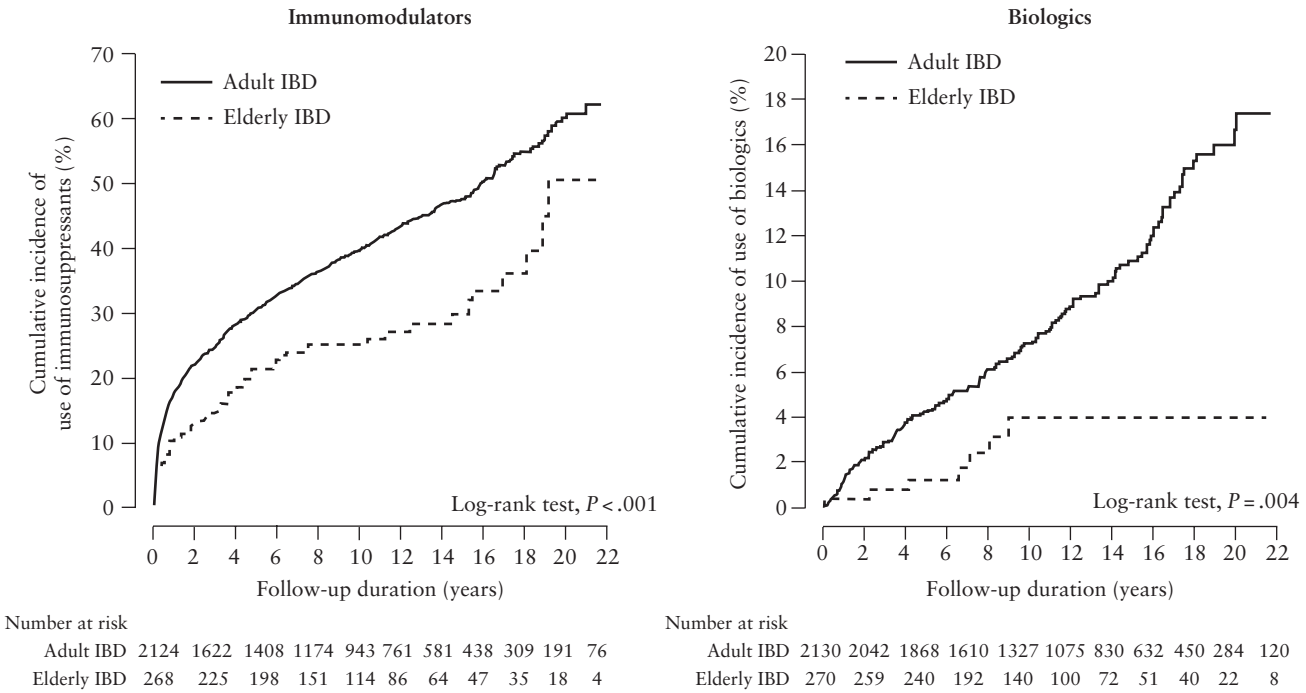
	Elderly-onset IBD [*n* = 270]	Adult-onset IBD [*n* = 2143]	*p*-value
Age at diagnosis	68.07 ± 6.7	36.12 ± 12.53	<0.0001
Male [*n*, %]	156 [57.8%]	1286 [60%]	0.510
Types of IBD [*n*, %]			
Crohn's disease [%]	56 [20.7%]	896 [41.8%]	<0.0001
Ulcerative colitis/IBD-undifferentiated [%]	214 [79.3%]	1247 [58.2%]	<0.0001
Family history of IBD	4 [1.9%]	58 [3.1%]	0.518
Current smokers/ex-smokers	96 [39.3%]	441 [22%]	<0.0001
dDrinkers/ex-drinkers	38 [16.8%]	163 [8.8%]	<0.0001
Comorbidities [*n*, %]			
Ischaemic heart disease	32 [11.9%]	40 [1.9%]	<0.0001
Stroke	15 [5.6%]	19 [0.9%]	<0.0001
Chronic obstructive pulmonary disease	16 [5.9%]	7 [0.3%]	<0.0001
Chronic kidney disease	4 [1.5%]	21 [1%]	0.516
Diabetes mellitus	49 [18.1%]	100 [4.7%]	<0.0001
Hypertension	120 [44.4%]	200 [9.3%]	<0.0001
History of cancer	45 [16.7%]	129 [6%]	<0.0001
Hepatitis B carrier	13 [9.1%]	121 [8.4%]	0.753
Hepatitis C carrier	1 [1.1%]	8 [0.8%]	0.527
Liver cirrhosis	5 [1.9%]	29 [1.4%]	0.579
Crohn's disease [*n* = 952]			
Disease location at diagnosis [*n*, %]			
L1 [ileal]	17 [30.4%]	214 [23.9%]	0.265
L2 [colonic]	17 [30.4%]	282 [31.5%]	1.000
L3 [ileocolonic]	22 [39.3%]	400 [44.6%]	0.489
L4 [Upper gastrointestinal]	7 [12.5%]	75 [8.4%]	0.320
Perianal	3 [5.4%]	228 [25.4%]	<0.0001
Disease phenotype at diagnosis [*n*, %]			
B1 [Inflammatory]	36 [64.3%]	624 [69.6%]	0.455
B2 [Stricturing]	18 [32.1%]	184 [20.5%]	0.044
B3 [Penetrating]	5 [8.9%]	131 [14.6%]	0.324
Ulcerative colitis [*n* = 1391]			
Disease location at diagnosis [*n*, %]			
E1 [Proctitis]	74 [37.4%]	427 [35.8%]	0.690
E2 [Left-sided colitis]	63 [31.8%]	347 [29.1%]	0.449
E3 [Pancolitis]	61 [30.8%]	419 [35.1%]	0.259
Medication used at diagnosis [*n*, %]			
5-Aminosalicyalates	185 [71.2%]	1473 [75.9%]	0.107
Steroids	62 [23.8%]	578 [29.8%]	0.050
Immunomodulators	18 [6.9%]	197 [10.2%]	0.119
Biologics	1 [0.4%]	6 [0.3%]	0.586

Percentages were based on non-missing data. Age was expressed in mean ± standard deviation. Qualitative and quantitative differences between subgroups were analysed by chi square or Fisher's exact tests for categorical parameters and Mann-Whitney testing for continuous parameters, as appropriate.

perceived safety of 5-ASAs, and perceived risks of immunosuppressants and biologic therapies in elderly patients.

The incidence of IBD is increasing rapidly in many newly industrialised countries in Asia. There has been a 30-fold increase in the incidence of IBD in the past 30 years, from 0.10 per 100 000 population to 3.12 per 100 000 in 2014.[23] We demonstrated that there has been nearly a 9-fold increase in incidence of elderly-onset IBD in Hong Kong, with incidences of 1.25 and 0.46 per 100 000 population in UC and CD, respectively, in years 2011–15. A previous population-based study by Lakatos *et al*. revealed that there had been a 10-fold increase in the incidence rate of elderly-onset UC in Western Hungary from 1977–81 to year 2002–08.[24] The rapid increase in elderly-onset IBD creates a significant burden on the health care system. It is estimated that one out of every 160 elderly over the age of 64 will be living with IBD in Canada in 2030.[4] Together with the ageing of the IBD population and the rapid increase in IBD incidence in newly industrialised countries, it will be expected that our health care system will be taking care of an IBD population with complex comorbidities. The budgetary effects caused by this compounding prevalence of IBD is substantial on our health care system.[25]

Similar to previous reported population-based studies in the West, we reported a significantly higher proportion of UC.[26,27] We also noted a significantly lower proportion of elderly-onset CD patients having perianal involvement, which is congruent with a recent systematic review and meta-analysis.[9] Data from the French EPIMAD population-based cohort revealed that the cumulative incidence of perianal CD was 9% at diagnosis of elderly-onset CD.[28] Another study in South Korea also showed that a similar percentage with 8% of elderly-onset CD patients presented with perianal involvement at diagnosis.[12] The lower prevalence of perianal involvement in elderly-onset CD might be due to different genetic predisposition. For example, the NOD2 gene is associated with earlier age at diagnosis and development of penetrating



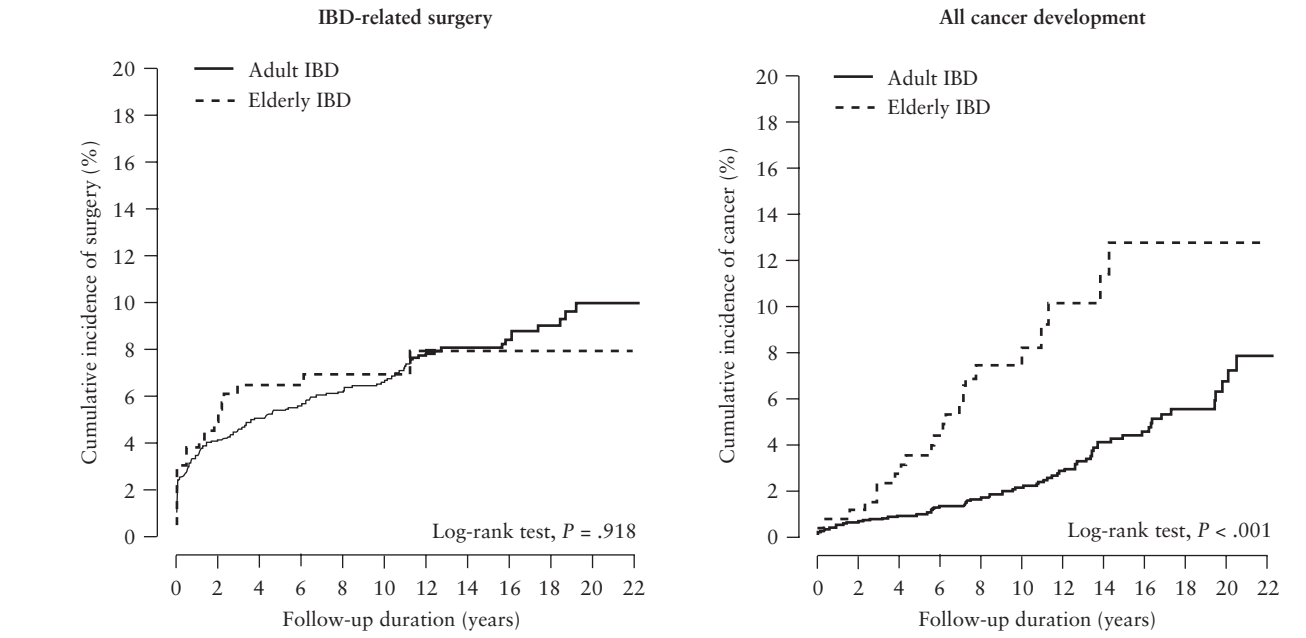
Number at risk

Adult IBD	2124	1622	1408	1174	943	761	581	438	309	191	76
Elderly IBD	268	225	198	151	114	86	64	47	35	18	4

Number at risk

Adult IBD	2130	2042	1868	1610	1327	1075	830	632	450	284	120
Elderly IBD	270	259	240	192	140	100	72	51	40	22	8

Figure 3. Cumulative probabilities of immunomodulators and biologics use in elderly-onset IBD and adult-onset inflammatory bowel disease [IBD] patients.



Number at risk

Adult IBD	2143	1973	1907	1683	1399	1154	905	695	506	342	189	36
Elderly IBD	270	249	237	208	157	111	81	70	54	32	15	3

Number at risk

Adult IBD	2121	2108	2052	1811	1504	1239	979	744	542	361	200	35
Elderly IBD	258	255	245	210	156	113	82	69	51	31	16	3

Figure 4. Cumulative probabilities of IBD-related surgeries and all-cancer develoment in elderly-onset IBD and adult-onset inflammatory bowel disease [IBD] patients.

complications.[29,30] This might explain why elderly-onset patients had less perianal CD. Perianal CD in adult-onset CD is much more prevalent in Asian populations compared with Caucasian populations.[31] However, in our study, only 5.4% of elderly-onset CD patients had perianal involvement. Whether it is due to genetic difference from adult-onset IBD remains uncertain. However, it is believed that genetics plays a less important role in the pathophysiology of IBD; rather, the gut microbiota might be related to the differences in disease phenotypes of IBD between the elderly and adults. In fact, the elderly have decreased abundance of anaerobes, eg, *Bifidobacteria*,[32] which was also found in the rectal mucosa of patients with perianal Crohn's fistula.[27]

Table 2. Risks of opportunistic infections, cancer development and hospitalisations in elderly-onset inflammatory bowel disease [IBD] compared with adult-onset IBD patients.

	Odds ratio [95% confidence interval]	*p*-value
Opportunistic infections		
Cytomegalovirus colitis	3.07[1.92–4.89]	<0.001
Herpes zoster	2.42[1.22–4.78]	0.012
Tuberculosis	1.45[0.60–3.50]	0.405
Clostridium difficile	0.81[0.29–2.29]	0.693
Hospitalisations within first 2 years of IBD diagnosis		
Overall number of hospitalisations	1.14[1.09–1.20]	<0.001
Infections-related hospitalisation	1.87[1.47–2.38]	<0.001
IBD-related hospitalisation	1.09[1.04-1.15]	0.001
Overall length of stay	1.004[1.001-1.007]	0.007
	Hazard ratio [95% confidence interval]	*p*-value
All-cancer development after IBD diagnosis[a]	1.82 [1.16–2.85]	0.010
All-cause mortality	7.92 [4.57–13.72]	<0.001

[a]Hazard ratio for all-cancer development has been adjusted for gender, smoking history, and alcohol history.

We also noted that a higher proportion of elderly-onset CD patients had stricturing phenotype compared with adult-onset CD patients. Patients with ileal CD were reported with higher risks of having a stricturing phenotype.[33] Our results indicated that more elderly-onset CD patients had ileal CD [30.4%] in comparison with adult-onset CD patients [23.9%], although this was not statistically significant. This might account for the higher proportion of elderly CD patients with the stricturing phenotype. In contrast to previous studies, we did not show an increase in colonic CD in elderly-onset CD patients.[34]

We demonstrated that the risk of IBD-related surgeries was not statistically significantly different between elderly-onset and adult-onset IBD patients; however, there was significantly less frequent use of immunomodulators and biologicsin elderly-onset IBD compared with adult-onset IBD. A recent systematic review revealed that the cumulative risks of surgery at 5 years in elderly-onset CD was 23% and in elderly-onset UC was 8%.[10] In Hong Kong, we showed that the cumulative risks of surgery at 5 years in elderly-onset CD was 18.9% and in elderly-onset UC was 3.6%, which were lower than those reported in the West. Cumulative exposure to immunomodulators and biologic agents were reported to be 38–64% lower in elderly-onset IBD patients.[10] Advanced age is associated with increased incidence rates of serious and opportunistic infections compared with younger patients.[35–37] Besides, the risk of thiopurine-associated lymphoma also increased in the elderly, with a relative risk of 4.78 in patients older than 50 years.[38] This might explain the lower use of immunomodulators and biologics in elderly-onset IBD. Besides, polypharmacy, which is common among the elderly, was significantly associated with increased risks of infection.[37] The overall utilisation of biological therapy is low in Hong Kong, due to its high cost and lack of insurance coverage. Previous data showed that only 11% of CD patients had received anti-TNF therapy in a university hospital in Hong Kong.[39]

We have also shown that, within the first 2 years of IBD diagnosis, elderly-onset IBD patients had almost a 2-fold increase in the risk of infections-related hospitalisation and increased risks of opportunistic infections, including CMV colitis and herpes zoster. However, the cumulative rates of surgeries between elderly-onset and adult-onset IBD are not significantly different statistically, and elderly-onset IBD patients had more IBD-related hospitalisations, indicating that disease course of elderly-onset IBD is not less complicated than that of adult-onset IBD. Elderly-onset IBD was also associated with higher risk of cancer development [HR: 1.82; 95% CI 1.16–2.85; $p = 0.010$] compared with non-elderly onset IBD patients after adjusting for gender and smoking and alcohol history. The higher risk of cancer in elderly-onset IBD patients could be explained by a significantly higher proportion of patients having diabetes mellitus and hypertension in the elderly-onset IBD cohort. Both diabetes mellitus and hypertension are positively associated with development of colorectal and breast cancers.[40,41]

This study has several strengths. As we used the data from a large territory-wide database which covered 95% of the IBD patients in Hong Kong, this addressed potential biases inherent in traditional cohort or observational studies. Moreover, as IBD is a chronic illness, the loss of follow-up rate in our database is low [<1%]. Furthermore, all cases of IBD were confirmed by investigators, which is important as IBD can often be mistaken for other differential diagnoses such as diverticulitis and ischaemic colitis.[29] However, there are several limitations. First, there was lack of clinical data and notes in the electronic database prior to the year 2000, and we were not able to capture all data relating to smoking, family history of IBD, and exact number of surgeries.

4.1. Conclusion

In conclusion, there has been a 9-fold increase in the incidence of elderly-onset IBD in Hong Kong over the past 30 years, with UC being four times more common than CD in the elderly. Despite significantly less use of immunomodulators and biologics, elderly-onset IBD has similar cumulative risks of surgery and higher numbers of overall hospitalisations compared with adult-onset IBD, indicating that elderly-onset IBD is at least as complicated as adult-onset IBD in the Chinese population. Further population-based studies are required to study the natural history and outcome of elderly-onset IBD in other ethnic groups. With the rapid increase in numbers of elderly-onset IBD and the ageing of current IBD patients, there is an urgent need to identify specific therapeutic strategies in this special group of patients.

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Conflict of Interest

JWYM reports grants from Janssen, the Hong Kong College of Physicians, and the Hong Kong Society of Gastroenterology, outside the submitted work. SCN reports grants from Ferring and personal fees from Takeda, AbbVie, Janssen, and Tillotts, outside the submitted work.

Author Contributions

Concept: JWYM, SCN. Methodology: JWYM, SCN, TCFY. Formal analysis: WYM TCFY. Funding acquisition: NSC. Data acquisition: WYM, CH,

WKL, ML, FHL, KMN, SFS, CML, SWCT, EHSS, KHC, BCYL, AJH, WHC. Writing—original draft: JWYM, CH. Writing—review and editing: NSC. Approval of final manuscript: all authors.

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