RISK OF ANAL CANCER IN INFLAMMATORY BOWEL DISEASE PATIENTS IN THE US: A POPULATION-BASED STUDY 2008–2018

Ryan Suk, Kalyani Sonawane, Cici Bauer, David Lairson, Ashish Deshmukh

Background: Patients with inflammatory bowel disease (IBD) are at elevated risk of developing anal cancer. However, it remains unclear whether the increased risk manifests from immunosuppressant use or location of the disease (inflammation). We aimed to examine whether the risk of anal cancer in IBD patients is attributable to immunosuppression or the disease's location by comparing IBD patients with rheumatoid arthritis (RA) and diverticulitis patients, respectively.

Methods: We conducted a retrospective cohort study using the US Optum® commercial claims database (2008–2018). We estimated the risk of anal cancer in the IBD cohort compared to the RA cohort (to examine risk attributable to immunosuppressant use) and the diverticulitis cohort (to examine risk attributable to similar disease location). Disease cohorts and index dates were identified using a combination of ICD diagnosis codes and prescription drug use. Patients 18 years and older and with a minimum of 12 months of continuous insurance enrollment were included. All three cohorts were mutually exclusive; we excluded persons with HIV/AIDS or organ transplant. We estimated hazard ratios (HRs) using Cox proportional regression, adjusting for age at diagnosis, comorbidity, risk factors for HPV infection (smoking, obesity, genital wart, substance abuse, alcoholism), and prescription drug use. Analyses were stratified by sex.

Results: The study included 70,314 patients with IBD, 164,991 with RA, and 129,558 with diverticulitis. In men, the adjusted hazard ratio (aHR) of developing anal cancer was 6.78 (95% CI, 3.40–13.55) comparing IBD to RA, and was 2.68 (95% CI, 0.99–7.30) comparing IBD to diverticulitis. Among women, the risk of developing anal cancer was significantly higher in IBD compared to RA (aHR 2.70; 95% CI, 1.36–5.35), but not different compared to diverticulitis (aHR 0.70; 95% CI, 0.20–2.44). The factors associated with a higher risk of anal cancer in both men and women were age at diagnosis, history of genital wart, corticosteroid use, and immunosuppressant use.

Conclusion: We found a significantly elevated risk of anal cancer in IBD patients than RA patients. However, anal cancer risk was not significantly different when comparing IBD patients to diverticulitis patients. These results indicate that the location of the disease is more strongly associated with anal cancer incidence than the treatment of autoimmune disease.

Factors associated with anal cancer incidence (IBD vs non-IBD cohorts), Men

	IBD vs RA	IBD vs Diverticulitis
	HR (95% CI)	HR (95% CI)
Men		
IBD (yes vs no)	6.78 (3.40-13.55)	2.68 (0.99-7.30)
Age at diagnosis (+1)	1.04 (1.03-1.06)	1.05 (1.04-1.07)
Comorbidity score (+1)	0.89 (0.78-0.99)	0.95 (0.85-1.05)
Smoking (yes vs no)	1.17 (0.52-2.63)	1.35 (0.64-2.83)
Obesity (yes vs no)	1.44 (0.70-2.95)	1.32 (0.67-2.59)
Genital wart (yes vs no)	12.11 (2.94-49.90)	13.05 (3.16-53.87)
Substance abuse (yes vs no)	NA	NA
Alcoholism (yes vs no)	0.68 (0.10-4.43)	NA
Corticosteroid (yes vs no)	1.90 (1.07-3.38)	2.09 (1.00-4.39)
Immunosuppressant (yes vs no)	1.22 (0.72-2.06)	1.62 (0.87-3.02)
5-ASA (yes vs no)	1.04 (0.63-1.73)	1.20 (0.67-2.16)
Anti-TNF-alpha (yes vs no)	1.83 (0.99-3.38)	2.81 (1.40-5.64)
Other drugs (yes vs no)	2.09 (1.17-3.75)	2.00 (1.06-3.79)

IBD, inflammatory bowel disease; RA, rheumatoid arthritis; HR, hazard ratio; CI, confidence interval; NA, not applicable

Factors associated with anal cancer incidence (IBD vs non-IBD cohorts), Women

	IBD vs RA	IBD vs Diverticulitis
	HR (95% CI)	HR (95% CI)
Women		
IBD (yes vs no)	2.70 (1.36-5.35)	0.70 (0.20-2.44)
Age at diagnosis (+1)	1.04 (1.02-1.05)	1.04 (1.02-1.06)
Comorbidity score (+1)	0.96 (0.88-1.06)	0.91 (0.83-0.99)
Smoking (yes vs no)	1.23 (0.59-2.55)	1.88 (1.01-3.53)
Obesity (yes vs no)	0.67 (0.35-1.30)	0.55 (0.25-1.18)
Genital wart (yes vs no)	13.40 (3.24-55.44)	7.14 (0.99-51.54)
Substance abuse (yes vs no)	1.96 (0.81-4.77)	1.63 (0.52-5.10)
Alcoholism (yes vs no)	0.74 (0.10-5.66)	0.80 (0.10-6.29)
Corticosteroid (yes vs no)	1.39 (0.89-2.18)	4.06 (1.26-13.07)
Immunosuppressant (yes vs no)	1.50 (0.99-2.26)	2.66 (1.35-5.23)
5-ASA (yes vs no)	1.07 (0.60-1.93)	0.77 (0.41-1.48)
Anti-TNF-alpha (yes vs no)	0.71 (0.34-1.47)	0.53 (0.12-2.37)
Other drugs (yes vs no)	1.70 (0.96-3.02)	1.82 (0.83-3.96)

IBD, inflammatory bowel disease; RA, rheumatoid arthritis; HR, hazard ratio; CI, confidence interval; NA, not applicable

TREATMENT PATTERNS OF NEWLY DIAGNOSED PEDIATRIC ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS IN THE IMPROVECARENOW REGISTRY

Theresa Hunter, Wendy Komocsar, Richard Colletti, Chunyan Liu, Keith Benkov, Jennifer Dotson, Steven Steiner, Nanhua Zhang, Wallace Crandall

Objectives: The objective of this study was to assess current treatment patterns of pediatric ulcerative colitis (UC) and Crohn's disease (CD) patients, using data in the ImproveCareNow (ICN) registry.

Methods: Pediatric (2–17 years) patients in the United States who were newly diagnosed with UC or CD between June 1, 2013-December 31, 2019, who had their first recorded ICN visit within 6 months of diagnosis and who were actively followed for at least 12 months (± 90 days) were included in this study. Descriptive statistics of baseline patient demographics were summarized for the overall IBD patient population and separately for UC and CD. Treatment patterns (including use of corticosteroids, 5-aminosalicylic acid (5-ASA), 6-mercaptopurine/azathioprine (6-MP/AZA), methotrexate, tumor necrosis factor inhibitors (TNFi) [adalimumab, infliximab, certolizumab, golimumab, and their biosimilars], ustekinumab, vedolizumab, and other medications [natalizumab and tofacitinib]) were assessed at the initial baseline visit, and at 1-year and 3-year time points.

Results: A total of 6,504 pediatric IBD patients (UC=1,784; CD=4,720) were included in this study. Patients had a mean age at diagnosis of 13.0 years (UC=13.2; CD=12.9), 57.1% were male (UC=49.6%; CD=60.0%), and 81.0% were White (UC=81.2%; CD=81.0%) (Table 1). At the initial ICN visit, 46.4% of UC patients were prescribed a corticosteroid, while 19.8% received a 5-ASA, 12.6% received a TNFi, 10.4% received a 6-MP/AZA, 3.0% received methotrexate, and 0.3% received vedolizumab. At the initial visit, 40.2% of CD patients were prescribed a corticosteroid, while 29.1% received a TNFi, 18.5% received a 6-MP/AZA, 12.4% received methotrexate, and 3.3% received a 5-ASA. At the 1-year and 3-year time points, rates of 5-ASA and corticosteroid use decreased among UC patients; however, rates of 6-MP/AZA, methotrexate, and TNFi increased (Table 2). Similarly, at the 1-year and 3-year time points, rates of corticosteroids among CD patients decreased; however, rates of methotrexate and TNFi increased (Table 2). There was also an increase in use of ustekinumab and vedolizumab over time among UC and CD patients.

Conclusion: These results highlight the current treatment patterns of pediatric UC and CD patients in the United States. At the initial ICN visit, the 46% of UC and 40% of CD patients were receiving corticosteroids, however, at 1-year and 3-years after initial visit, over 30% of UC patients and over 60% of CD patients were receiving TNF inhibitors with considerably reduced corticosteroid use.

Table 1: Demographic and baseline characteristics

	CD (N=4720)	UC (N=1784)	Overall (N=6504)
Age at diagnosis in years			
N	4720	1784	6504
Min-Max	2.1-17.9	2.0-17.9	2.0-17.9
Mean (SD)	12.9 (3.14)	13.2 (3.57)	13.0 (3.27)
Median (Q1, Q3)	13.3 (10.9, 15.4)	14.1 (11.3, 15.9)	13.5 (11.0, 15.6)
Age group at diagnosis			
2 - 5	95 (2.0%)	60 (3.4%)	155 (2.4%)
6 - 11	1135 (24.0%)	357 (20.0%)	1492 (22.9%)
12 - 17	3490 (73.9%)	1367 (76.6%)	4857 (74.7%)
Gender			
Male	2833 (60.0%)	884 (49.6%)	3717 (57.1%)
Female	1887 (40.0%)	900 (50.4%)	2787 (42.9%)
Race			
Black	445 (12.2%)	134 (10.3%)	579 (11.7%)
White	2948 (81.0%)	1060 (81.2%)	4008 (81.0%)
Other	247 (6.8%)	112 (8.6%)	359 (7.3%)
Missing	1080	478	1558
Ethnicity			
Hispanic	187 (4.6%)	159 (10.4%)	346 (6.2%)
Non-Hispanic	3908 (95.4%)	1364 (89.6%)	5272 (93.8%)
Missing	625	261	886
Baseline* weight (kg)			
N	4663	1774	6437
Min-Max	10.3-141.0	11.7-144.3	10.3-144.3
Mean (SD)	45.2 (17.29)	51.3 (19.43)	46.9 (18.11)
Median (Q1, Q3)	43.4 (32.4, 55.9)	51.5 (37.9, 62.8)	45.7 (33.1, 58.2)
Baseline* height (cm)			
N	4648	1765	6413
Min-Max	81.4-198.1	87.6-198.1	81.4-198.1
Mean (SD)	152.4 (18.43)	155.1 (20.14)	153.1 (18.95)
Median (Q1, Q3)	154.8 (140.8, 166.0)	159.8 (145.4, 168.5)	156.1 (141.5, 166.8)

* Baseline is at enrollment

Table 2: Treatment pattern of pediatric UC and CD patients specified time points/intervals

Medication	Initial visit	1-year from initial visit	3-year from initial visit
Crohn's Disease			
	N=4720	N=4720	N=1920
5-ASA[1]	154 (3.3%)	120 (2.5%)	37 (1.9%)
Corticosteroid[2]	1898 (40.2%)	297 (6.3%)	71 (3.7%)
6-MP/AZA	873 (18.5%)	973 (20.6%)	321 (16.7%)
Methotrexate	584 (12.4%)	957 (20.3%)	403 (21.0%)
TNFi[3]	1375 (29.1%)	2846 (60.3%)	1285 (66.9%)
Ustekinumab	0	27 (0.6%)	42 (2.2%)
Vedolizumab	0	25 (0.5%)	30 (1.6%)
Other[4]	0	0	0
Ulcerative Colitis			
	N=1784	N=1784	N=599
5-ASA[1]	354 (19.8%)	258 (14.5%)	62 (10.4%)
Corticosteroid[2]	828 (46.4%)	229 (12.8%)	42 (7.0%)
6-MP/AZA	185 (10.4%)	364 (20.4%)	122 (20.4%)
Methotrexate	53 (3.0%)	144 (8.1%)	56 (9.3%)
TNFi[3]	225 (12.6%)	565 (31.7%)	232 (38.7%)
Ustekinumab			1 (0.2%)
Vedolizumab	6 (0.3%)	58 (3.3%)	39 (6.5%)
Other[4]		1 (0.1%)	3 (0.5%)

N=Number of patients at the start time point of the interval
[1]5-ASA: balsalazine, mesalamine
[2]Corticosteroid: prednisone, budesonide, methylprednisolone
[3]Tumor necrosis factor inhibitor (TNFi): infliximab, adalimumab, certolizumab, golimumab, and their biosimilars
[4]Other: natalizumab, tofacitinib

UNDERSTANDING REAL-WORLD BIOLOGIC MAINTENANCE DOSING PATTERNS AMONG PEDIATRIC ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS

Wallace Crandall, Richard Colletti, Wendy Komocsar, Chunyan Liu, Jennifer Dotson, Keith Benkov, Steven Steiner, Nanhua Zhang, Theresa Hunter

Objectives: To assess the initial and long-term maintenance dosing of biologic medications in pediatric UC and CD patients, using data in the ICN registry.

Methods: Pediatric patients (2–17 years) in the US who were diagnosed with UC or CD between June 1, 2013 and December 31, 2019, who, after enrollment in the ICN registry, initiated a biologic (adalimumab, infliximab, certolizumab, golimumab, ustekinumab, vedolizumab, and natalizumab) and were actively followed for at least 12 months after first maintenance dose were included in this study. Descriptive statistics of baseline patient demographics were summarized for the overall Inflammatory Bowel Disease (IBD) patient population and separately for UC and CD. Biologic maintenance dosage was calculated for UC and CD patients who had data for both dose and weight for each biologic at the baseline visit (first maintenance dose), 1-year and 3-year time points.

Results: A total of 1,887 pediatric IBD patients (UC=350; CD=1,537) were included in this study. Patients had a mean age at diagnosis of 12.9 years (UC=13.1; CD=12.9), 57.1% were male (UC=48.9%; CD=59.0%), and 80.6% were White (UC=79.8%; CD=80.8%) (Table 1). Infliximab (77.0%) was the most commonly prescribed biologic for UC, followed by adalimumab (12.4%), vedolizumab (10.1%), certolizumab (0.3%), and ustekinumab (0.3%). Similarly, infliximab (80.6%) was the most commonly prescribed biologic for CD, followed by adalimumab (16.5%), vedolizumab (1.6%), ustekinumab (1.2%), and certolizumab (0.1%) (Table 2).

At first maintenance dose, UC patients on infliximab were receiving a mean dose of 10.5mg/kg/8wk, patients on adalimumab (weight <40kg) were receiving a mean dose of 1.3mg/kg/2wk, patients on adalimumab (weight≥40kg) were receiving a mean dose of 0.8mg/kg/2wk, and patients on vedolizumab were receiving a mean dose of 6.9mg/kg/8wks. Mean dose of infliximab among UC patients increased from 10.5mg/kg/8wk at first maintenance dose to 11.8mg/kg/8wk at 1-year from first maintenance dose.

At the first maintenance dose, CD patients on infliximab were receiving a mean dose of 8.1mg/kg/8wk, patients on adalimumab (weight <40kg) were receiving a mean dose of 1.1mg/kg/2wk, patients on adalimumab (weight ≥40kg) were receiving a mean dose of 0.8mg/kg/2wk, patients receiving vedolizumab were receiving a mean dose of 10.5mg/kg/8wks. Mean dose of infliximab among CD patients increased from 8.1mg/kg/8wk at first maintenance dose to 9.6mg/kg/8wk at 1-year from first maintenance dose.

Conclusion: These results highlight the biologic maintenance dose changes among pediatric UC and CD patients. TNF inhibitors remain the most commonly used class of biologic, but the doses being used are double the standard dosing guidelines. There is little evidence of dose reduction over time among pediatric UC and CD patients in the ICN registry.

Table 1: Demographic and baseline characteristics

	CD (N=1,537)	UC (N=350)	Overall (N=1887)
Age at diagnosis in years			
Min-Max	2.1-17.9	3.2-17.9	2.1-17.9
Mean (SD)	12.9 (3.00)	13.1 (3.42)	12.9 (3.08)
Median (Q1, Q3)	13.2 (10.9, 15.3)	13.8 (11.3, 15.6)	13.3 (11.0, 15.3)
Age group at diagnosis			
2 – 5	21 (1.4%)	11 (3.1%)	32 (1.7%)
6 – 11	385 (25.0%)	69 (19.7%)	454 (24.1%)
12 – 17	1131 (73.6%)	270 (77.1%)	1401 (74.2%)
Gender			
Male	907 (59.0%)	171 (48.9%)	1078 (57.1%)
Female	630 (41.0%)	179 (51.1%)	809 (42.9%)
Race			
Black	157 (13.4%)	24 (9.5%)	181 (12.7%)
White	950 (80.8%)	201 (79.8%)	1151 (80.6%)
Other	69 (5.9%)	27 (10.7%)	96 (6.7%)
Missing	361	98	459
Ethnicity			
Hispanic	63 (4.7%)	33 (11.3%)	96 (5.8%)
Non-Hispanic	1287 (95.3%)	260 (88.7%)	1547 (94.2%)
Missing	187	57	244
Baseline* weight (kg)			
N	1513	346	1859
Min-Max	13.4-148.2	12.2-119.4	12.2-148.2
Mean (SD)	49.7 (17.96)	55.3 (18.96)	50.7 (18.28)
Median (Q1, Q3)	48.2 (36.3, 60.8)	55.2 (44.0, 67.2)	49.4 (37.3, 61.8)
Baseline* height (cm)			
N	1501	342	1843
Min-Max	97.5-190.8	95.3-188.7	95.3-190.8
Mean (SD)	154.7 (16.87)	158.0 (17.79)	155.3 (17.08)
Median (Q1, Q3)	157.0 (143.5, 167.0)	161.0 (150.6, 169.5)	157.8 (144.6, 167.6)

* Baseline is at biologic initiation

Table 2: Dosing interval of standardized biologic maintenance dose at the specified time points/intervals

Biologic agent	First Maintenance dose	1-year from first Maintenance dose	3-year from first Maintenance dose	Last recorded Maintenance dose for patients who did not discontinue
Crohn's Disease				
Infliximab (mg/kg/8 weeks)				
N[1]	1302	1049	313	982
N-miss[2]	31	71	19	7
Min-Max	0.2-31.5	1.8-41.5	2.5-31.4	0.4-41.5
Mean (SD)	8.1 (4.17)	9.6 (4.63)	10.0 (4.93)	10.4 (5.04)
Median (Q1, Q3)	6.6 (5.1, 9.8)	8.7 (5.9, 11.7)	9.3 (6.0, 12.6)	9.7 (6.7, 12.7)
Adalimumab (mg/kg/2 weeks) (weight < 40kg)				
N	66	33	3	21
N-miss	1	1	1	0
Min-Max	0.3-5.4	0.5-3.6	0.6-2.7	0.5-2.7
Mean (SD)	1.1 (0.68)	1.2 (0.59)	1.5 (1.12)	1.2 (0.64)
Median (Q1, Q3)	1.0 (0.7, 1.3)	1.1 (0.8, 1.3)	1.1 (0.6, 2.7)	1.1 (0.7, 1.4)
Adalimumab (mg/kg/2 weeks) (weight >= 40kg)				
N	201	180	26	174
N-miss	4	9	2	0
Min-Max	0.3-3.3	0.2-2.7	0.4-2.0	0.3-3.1
Mean (SD)	0.8 (0.32)	0.8 (0.38)	0.9 (0.38)	0.8 (0.36)
Median (Q1, Q3)	0.8 (0.6, 0.9)	0.7 (0.6, 0.9)	0.7 (0.6, 1.2)	0.7 (0.6, 0.9)
Certolizumab (mg/kg/4 weeks)				
N	2	2		1
N-miss	0	0		0
Min-Max	10.9-11.1	6.1-10.6		5.8-5.8
Mean (SD)	11.0 (0.12)	8.3 (3.22)		5.8 (.)
Median (Q1, Q3)	11.0 (10.9, 11.1)	8.3 (6.1, 10.6)		5.8 (5.8, 5.8)
Ustekinumab (mg/kg/8 weeks)				
N	19	15		13
N-miss	0	2		0
Min-Max	0.4-4.9	1.0-3.8		0.4-3.7
Mean (SD)	2.3 (1.21)	2.4 (1.00)		2.2 (1.18)
Median (Q1, Q3)	1.9 (1.4, 3.3)	2.4 (1.4, 3.4)		2.1 (1.3, 3.4)
Vedolizumab (mg/kg/8 weeks)				
N	26	19	3	18
N-miss	0	1	0	1
Min-Max	3.7-24.0	4.7-22.3	4.4-12.1	4.2-31.6
Mean (SD)	10.5 (6.17)	9.8 (5.13)	7.1 (4.33)	11.1 (6.72)
Median (Q1, Q3)	7.8 (5.8, 15.3)	7.3 (5.3, 13.0)	4.8 (4.4, 12.1)	10.6 (6.5, 13.5)
Ulcerative Colitis				
Infliximab (mg/kg/8 weeks)				
N[1]	291	212	43	192
N-miss[2]	6	15	4	3
Min-Max	2.2-44.0	4.2-37.9	4.7-21.2	4.2-25.8
Mean (SD)	10.5 (5.55)	11.8 (5.53)	11.0 (4.53)	11.2 (4.77)
Median (Q1, Q3)	9.4 (6.0, 13.0)	10.2 (8.3, 14.0)	9.8 (7.6, 14.3)	10.1 (7.9, 13.4)
Adalimumab (mg/kg/2 weeks) (weight < 40kg)				
N	5	1		
N-miss	0	0		
Min-Max	1.0-2.0	1.1-1.1		
Mean (SD)	1.3 (0.41)	1.1 (.)		
Median (Q1, Q3)	1.1 (1.1, 1.3)	1.1 (1.1, 1.1)		
Adalimumab (mg/kg/2 weeks) (weight >= 40kg)				
N	42	28	5	30
N-miss	0	2	0	0
Min-Max	0.5-1.7	0.4-1.9	0.5-1.1	0.4-1.8
Mean (SD)	0.8 (0.27)	0.9 (0.38)	0.8 (0.28)	0.9 (0.35)
Median (Q1, Q3)	0.7 (0.5, 0.9)	0.8 (0.6, 1.1)	0.6 (0.6, 1.0)	0.8 (0.6, 1.0)
Certolizumab (mg/kg/4 weeks)				
N	1	1	1	
N-miss	0	0	0	
Min-Max	4.4-4.4	3.8-3.8	3.2-3.2	
Mean (SD)	4.4 (.)	3.8 (.)	3.2 (.)	
Median (Q1, Q3)	4.4 (4.4, 4.4)	3.8 (3.8, 3.8)	3.2 (3.2, 3.2)	
Ustekinumab (mg/kg/8 weeks)				
N	1	1		1
N-miss	0	0		0
Min-Max	2.8-2.8	2.9-2.9		2.9-2.9
Mean (SD)	2.8 (.)	2.9 (.)		2.9 (.)
Median (Q1, Q3)	2.8 (2.8, 2.8)	2.9 (2.9, 2.9)		2.9 (2.9, 2.9)
Vedolizumab (mg/kg/8 weeks)				
N	38	30	1	29
N-miss	0	1	0	0
Min-Max	2.0-15.7	2.5-21.7	9.9-9.9	2.8-16.3
Mean (SD)	6.9 (2.88)	7.2 (4.33)	9.9 (.)	6.6 (3.66)
Median (Q1, Q3)	6.2 (4.8, 8.7)	5.8 (4.2, 10.6)	9.9 (9.9, 9.9)	5.7 (4.1, 6.8)

[1]N is the number of patients on the specific biologic who had maintenance dose data at the specified time points.
[2]N-miss is the number of patients on the specific biologic at the specified time points but had missing data in maintenance dose.
No patient was on Golimumab or Natalizumab.

Epithelial Cell Biology/Function in Inflammation

ADENOSINE A3 RECEPTOR INTERACTS WITH GASDERMIN D TO MODULATE INTESTINAL EPITHELIAL CELL PYROPTOSIS IN ULCERATIVE COLITIS

Peng Xiao, Minmin Lv, Wenke Chen, Ting Tian, Tianhua Ren

Background: Adenosine A3 receptor (A3AR) plays a role in intestinal inflammation, but little is known about its mechnisms in intestinal inflammation such as ulcerative colitis (UC). Pyroptosis, characterized by Gasdermin D (GSDMD) activation, is implicated in the pathogenesis of UC. We investigated the role of A3AR in GSDMD-mediated pyroptosis in UC and its underlying molecular mechanisms.

Methods: The expression of A3AR in colonic mucosa of patients with UC were examined. A3AR agonist was used to study the role of A3AR in ex vivo colonic explants of UC patients. In addition, human intestinal epithelial cells Caco-2 were used to further verify the effect of A3AR on pyroptosis induced by LPS+ATP. RT-qPCR and western blotting were used to detect the expression levels of pyroptosis-associated factors including NLRP3, caspase-1, gasdermin-D N-terminal domain (GSDMD-NT), IL-1β and IL-18 in colonic tissues and Caco-2 cells. Immunofluorescence was used to detect the protein expression in tissues and cells. Enzyme-linked immunosorbent assay was used to determine the levels of IL-1β and IL-18 in tissue and cell culture