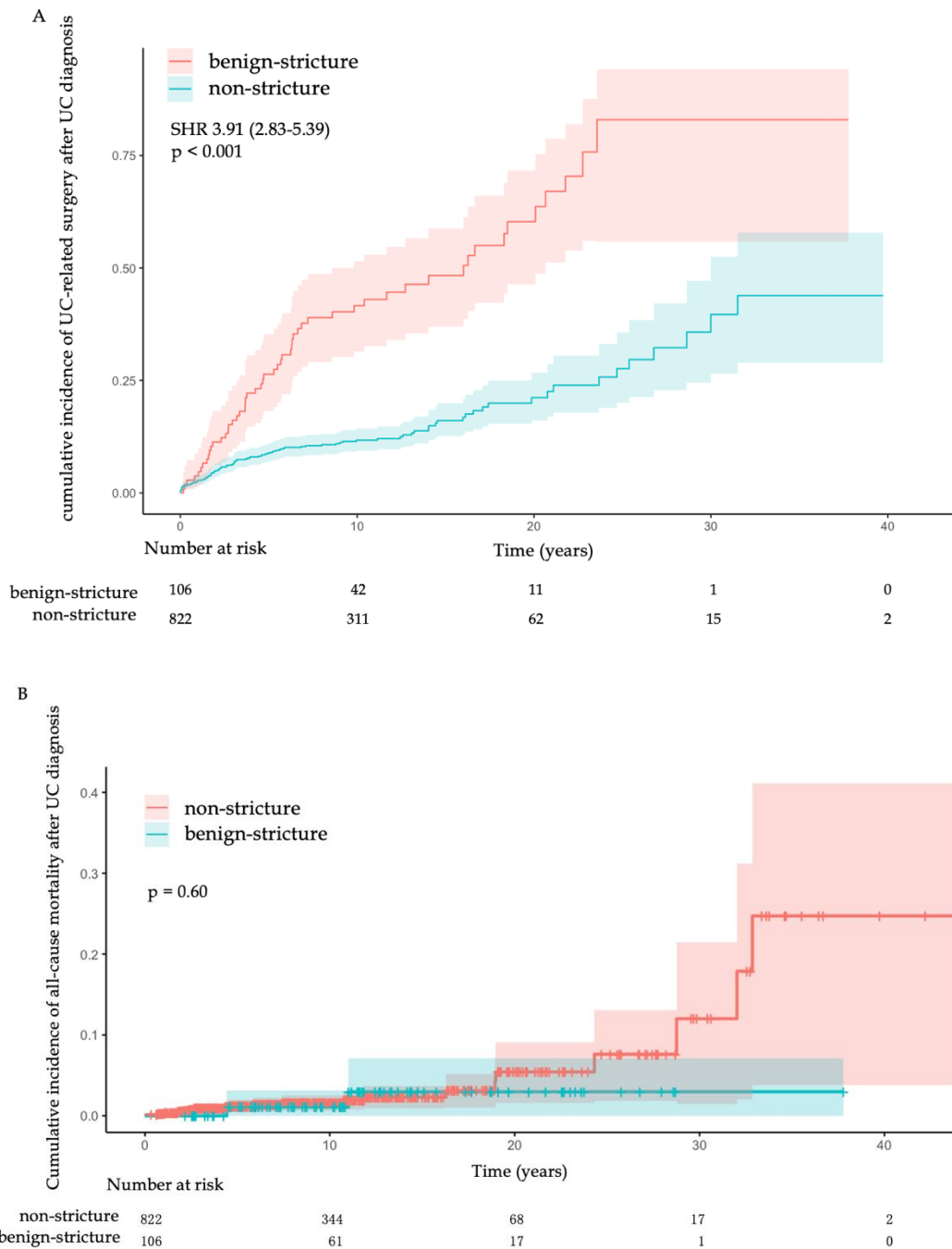


Supplementary Figure 1 Cumulative incidence of ulcerative colitis-related surgery, colorectal cancer, and all-cause mortality in the stricture group and non-stricture group (excluding referred surgical cases and patients undergoing surgery within 30 days of diagnosis). A: Fine-Gray competing risk model analysis of UC-related surgery; B: Fine-Gray competing risk model analysis of CRC; C: Kaplan-Meier analysis of all-cause mortality. UC: ulcerative colitis; CRC: colorectal cancer; SHR: subdistribution hazard ratio.



Supplementary Figure 2 Cumulative incidence of ulcerative colitis-related surgery and all-cause mortality in the benign-stricture group and non-stricture group. A: Fine-Gray competing model of UC-related surgery; B: Kaplan-Meier analysis of all-cause mortality. UC: ulcerative colitis; SHR: Subdistribution hazard ratio.

Supplementary Table 1 Missing data for key variables of the study population

	All cases	Malignant stricture group	Benign stricture group	Non-stricture group
Number of patients	938	10	106	822
Montreal classification (%)	7 (0.74%)	0 (0.0%)	0 (0.0%)	7 (0.85%)
Weight loss (%)	4 (0.42%)	0 (0.0%)	0 (0.0%)	4 (0.48%)
Hemoglobin (%)	1 (0.10%)	0 (0.0%)	0 (0.0%)	1 (0.12%)
Albumin (%)	1 (0.10%)	0 (0.0%)	0 (0.0%)	1 (0.12%)
CRP (%)	5 (0.53%)	0 (0.0%)	1 (0.94%)	4 (0.48%)
ESR (%)	24 (2.55%)	3 (30.00%)	3 (2.83%)	18 (2.18%)
Clinical activity until surgery or the end of follow-up (%)	32 (3.41%)	0 (0.0%)	6 (5.66%)	26 (3.16%)
Location of stricture (%)	-	0 (0.0%)	8 (5.97%)	-

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

Supplementary Table 2 Clinical features and outcomes of improved stricture group and persistent stricture group

	All stricture cases	Improved stricture	Persistent stricture	<i>P</i> value
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Number of patients	96	8	88	
Number of strictures (%)				0.399
1	79 (82.3%)	8 (100.0%)	71 (80.7%)	
2	16 (16.7%)	0 (0.0%)	16 (18.2%)	
3	1 (1.0%)	0 (0.0%)	1 (1.1%)	
Male (%)	47 (49.0%)	3 (37.5%)	44 (50.0%)	0.758
Median duration from diagnosis to stricture, yr (median, IQR)	5.14 (2.49-12.37)	2.54 (1.86-3.56)	5.61 (2.86-12.76)	0.019
Endoscopic passability (%)				0.861
Colonoscope passable	32 (33.3%)	2 (25.0%)	30 (34.1%)	
Gastroscope passable	20 (20.8%)	2 (25.0%)	18 (20.5%)	
Impassable by both	44 (45.8%)	4 (50.0%)	40 (45.5%)	
Location of the stricture (%)				0.056
Rectum	25 (21.9%)	0 (0.0%)	25 (23.6%)	
the Left colon	72 (63.2%)	5 (62.5%)	67 (63.2%)	
the Right colon	17 (14.9%)	3 (37.5%)	14 (13.2%)	

Symptomatic large bowel obstruction (%)	20 (20.8%)	0 (0.0%)	20 (22.7%)	0.289
Treatment after the stricture formation (%)				
5-ASA	74 (77.1%)	7 (87.5%)	67 (76.1%)	0.770
Systemic glucocorticoids	41 (42.7%)	5 (62.5%)	36 (40.9%)	0.419
Immunomodulators	14 (14.6%)	1 (12.5%)	13 (14.8%)	1.000
Anti-TNF- α	13 (13.5%)	1 (12.5%)	12 (13.6%)	1.000
VDZ	25 (26.0%)	4 (50.0%)	21 (23.9%)	0.233
Clinical activity until surgery or the end of follow-up (%)				0.146
Clinical remission	30 (31.3%)	3 (37.5%)	27 (30.7%)	
Mild activity	25 (26.0%)	4 (50.0%)	21 (23.9%)	
Moderate activity	26 (27.1%)	1 (12.5%)	25 (28.4%)	
Severe activity	15 (15.6%)	0 (0.0%)	15 (17.0%)	
UC-related surgery (%)	45 (46.9%)	0 (0.0%)	45 (51.1%)	0.016
CRC (%)	8 (8.3%)	0 (0.0%)	8 (9.1%)	1.000

Severe intestinal complications (%)	34 (35.4%)	1 (12.5%)	33 (37.5%)	0.303
Bleeding	6 (6.3%)	1 (12.5%)	5 (5.7%)	0.415
Perforation	5 (5.2%)	0 (0.0%)	5 (5.7%)	1.000
Obstruction	20 (20.8%)	0 (0.0%)	20 (22.7%)	0.289
Fistula	3 (3.1%)	0 (0.0%)	3 (3.4%)	1.000
Toxin megacolon	3 (3.1%)	0 (0.0%)	3 (3.4%)	1.000
All-cause mortality (%)	4 (4.2%)	0 (0.0%)	4 (4.5%)	1.000

IQR: interquartile range; 5-ASA: 5-aminosalicylic; anti-TNF- α : anti-tumor necrosis factor α ; VDZ: vedolizumab; UC: ulcerative colitis; CRC: colorectal cancer.

Supplementary Table 3 Multivariate time- dependent cox analysis of risk factors for persistent stricture formation in UC

Variables	Univariate		Multivariate	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Median time from diagnosis to stricture	1.022 (0.996-1.049)	0.095	1.019 (0.991-1.047)	0.166
Location of the stricture		0.276		0.405
Rectum	1		1	

the Left colon	0.781 (0.463-1.316)	0.353	0.856 (0.498-1.471)	0.574
the Right colon	0.556 (0.268-1.153)	0.114	0.613 (0.292-1.289)	0.197
Endoscopic passability		0.746		
Colonoscopy passable	1			
Gastroscope passable	0.896 (0.499-1.609)	0.715		
Impassable by both	0.920 (0.573-1.478)	0.732		
Symptomatic large bowel obstruction	1.371 (0.830-2.266)	0.216		
Treatment after the stricture formation				
Systemic glucocorticoids	0.957 (0.575-1.590)	0.865		
Immunomodulators	1.301 (0.527-3.213)	0.567		
Anti-TNF- α	1.290 (0.317-5.246)	0.721		
VDZ	0.833 (0.363-1.909)	0.665		

UC: ulcerative colitis; HR: hazard ratio; CI: confidence interval; anti-TNF- α : anti-tumor necrosis factor α ; VDZ: vedolizumab.

Supplementary Table 4 Basic information and clinical characteristics of the study population (complete-case analysis)

	Stricture group			Non-stricture group	<i>P</i> ¹
	All stricture cases	Malignant stricture group	Benign stricture group		
Number of patients	116	10	106	822	
Montreal classification (%)					0.060
E1 (proctitis)	23 (19.8%)	0 (0.0%)	23 (21.7%)	102 (12.5%)	
E2 (left-sided colitis)	28 (24.2%)	3 (30.0%)	25 (23.6%)	251 (30.8%)	
E3 (pancolitis)	65 (56.0%)	7 (70.0%)	58 (54.7%)	462 (56.7%)	
Weight loss (%)	81 (69.8%)	6 (60.0%)	75 (70.8%)	540 (66.0%)	0.416
Hemoglobin, g/L (mean ± SD)	103.78±23.59	108.10±20.43	103.38±23.91	111.64±26.28	<0.001
CRP, mg/L (median, IQR)	11.43 (2.20, 43.87)	4.61 (2.57, 20.35)	12.33 (2.0, 44.60)	9.12 (2.07, 33.03)	0.401
ESR, mm/h (median, IQR)	23 (12, 48)	15 (7, 16)	27 (12, 49)	20 (9, 40)	0.124
Clinical activity until					<0.001

surgery or the end of follow-up (%)				
Clinical remission	28 (24.1%)	3 (30.0%)	25 (25.0%)	352 (44.2%)
Mild activity	25 (22.7%)	6 (60.0%)	19 (19.0%)	217 (27.3%)
Moderate activity	34 (30.9%)	1 (10.0%)	33 (33.0%)	128 (16.1%)
Severe activity	23 (20.9%)	0 (0.0%)	23 (23.0%)	99 (12.4%)
Location of the stricture (%)	0.045			
Rectum	30 (24.0%)	4 (34.4%)	26 (22.6%)	
Left colon	77 (61.1%)	3 (27.3%)	74 (64.3%)	
Right colon	19 (15.2%)	4 (36.4%)	15 (13.0%)	

¹Statistical comparisons were conducted between stricture and non-stricture groups.

UC: ulcerative colitis; SD: standard deviation; IQR: interquartile range; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

Supplementary Table 5 Multivariate Cox regression analysis of risk factors for colorectal stricture formation in UC (complete-case analysis)

Variables	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value

Male	0.896 (0.621-1.293)	0.557		
Age at diagnosis \geq 40 yr	2.273 (1.562-3.308)	<0.001	2.099 (1.409-3.128)	<0.001
Montreal classification		0.080		0.355
E1 (proctitis)	1		1	
E2 (left-sided colitis)	0.558 (0.321-0.969)	0.038	0.658 (0.367-1.181)	0.161
E3 (pancolitis)	0.855 (0.530-1.377)	0.518	0.840 (0.505-1.401)	0.505
Extraintestinal involvement	2.077 (1.346-3.205)	<0.001	2.030 (1.287-3.203)	0.002
Hemoglobin	0.986 (0.979-0.992)	<0.001	0.987 (0.979-0.995)	<0.001
CRP	1.007 (1.002-1.011)	0.003	1.004 (0.999-1.010)	0.141
ESR	1.008 (1.001-1.015)	0.023	0.996 (0.987-1.006)	0.413
Treatment until stricture or the end of follow-up				
5-ASA	0.406 (0.163-1.012)	0.053	0.169 (0.059-0.481)	<0.001
Systemic glucocorticoids	1.895 (1.145-3.135)	0.013	2.794 (1.477-5.286)	0.002
Immunomodulators	0.985 (0.654-1.482)	0.942		
Anti-TNF- α	0.764 (0.450-1.298)	0.320	0.854 (0.476-1.529)	0.595
VDZ	0.370 (0.199-0.689)	0.002	0.395 (0.209-0.746)	0.004

UST	0.049 (0.0-5887.28)	0.614	0.000(0.0-2.04E+161)	0.961
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UC: ulcerative colitis; HR: hazard ratio; CI: confidence interval; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; 5-ASA: 5-aminosalicylic; anti-TNF- α : anti-tumor necrosis factor α ; VDZ: vedolizumab; UST: Ustekinumab

Supplementary Table 6 Multivariate Cox regression analysis of risk factors for benign colorectal stricture formation in UC

Variables	Univariate		Multivariate	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Male	0.830 (0.566-1.217)	0.341		
Age at diagnosis \geq 40 yr	2.255 (1.528-3.327)	<0.001	2.161 (1.444-3.234)	<0.001
Montreal classification		0.050		0.130
E1 (proctitis)	1		1	
E2 (left-sided colitis)	0.501 (0.284-0.882)	0.017	0.552 (0.309-0.986)	0.045
E3 (pancolitis)	0.768 (0.473-1.247)	0.286	0.695 (0.422-1.145)	0.153
Extraintestinal involvement	1.964 (1.243-3.101)	0.004	1.919 (1.198-3.074)	0.007
Hemoglobin	0.985 (0.978-0.992)	<0.001	0.987 (0.979-0.995)	0.001
CRP	1.007 (1.003-1.012)	0.002	1.004 (0.999-1.010)	0.126
ESR	1.009 (1.002-1.016)	0.014	0.996 (0.986-1.005)	0.388

Treatment until stricture or the end of follow-up				
5-ASA	0.360 (0.144-0.900)	0.029	0.173 (0.061-0.495)	0.001
Systemic glucocorticoids	2.102 (1.216-3.632)	0.008	2.730 (1.438-5.181)	0.002
Immunomodulators	0.999 (0.654-1.527)	0.997		
Anti-TNF- α	0.798 (0.469-1.360)	0.407	0.947 (0.536-1.675)	0.852
VDZ	0.392 (0.210-0.732)	0.003	0.398 (0.211-0.753)	0.005
UST	0.049 (0.0-5643.18)	0.612	0.000(0.0-4.1E+165)	0.961

UC: ulcerative colitis; HR: hazard ratio; CI: confidence interval; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; 5-ASA: 5-aminosalicylic; anti-TNF- α : anti-tumor necrosis factor α ; VDZ: vedolizumab; UST: Ustekinumab.

Supplementary Table 7 Basic information and prognostic outcomes of the study population (excluding referred surgical cases and patients undergoing surgery within 30 days of diagnosis)

Stricture group				Non-stricture group	P^1
All stricture cases	Malignant stricture group	Benign stricture group			

Number of patients	91	6	85	786	
Male (%)	48 (52.7%)	4 (66.7%)	44 (51.8%)	446 (56.7%)	0.467
Age at diagnosis, yr (median, IQR)	38.48 (28.71-49.06)	36.06 (32.19-42.39)	39.44 (28.69-50.98)	34.29 (26.39-46.64)	0.045
≥40	44 (48.4%)	2 (33.3%)	42 (49.4%)	289 (37.7%)	0.031
Disease duration, yr (median, IQR)	10.67 (6.75-16.67)	25.39 (19.38-32.39)	10.26 (6.48-14.93)	9.00 (5.65-13.39)	0.009
Follow-up time, yr (median, IQR)	8.09 (4.24-15.76)	24.10 (19.17-32.37)	7.20 (3.67-13.86)	8.67 (4.84-12.67)	0.740
Montreal classification (%)					0.114
E1 (proctitis)					
	17 (18.7%)	0 (0.0%)	17 (20.0%)	99 (12.6%)	
E2 (left-sided colitis)	21 (23.1%)	1 (16.7%)	20 (23.5%)	249 (31.7%)	
E3 (pancolitis)	53 (58.2%)	5 (83.3%)	48 (56.5%)	438 (55.7%)	
Smoking status (%)					0.876
Active smoker					
	6 (6.6%)	0 (0.0%)	6 (7.1%)	54 (6.9%)	

Former smoker	15 (16.5%)	0 (0.0%)	15 (17.6%)	146 (18.6%)	
Nonsmoker	70 (76.9%)	6 (100.0%)	64 (75.3%)	586 (74.6%)	
Family history of IBD (%)	4 (4.4%)	1 (16.7%)	3 (3.5%)	37 (4.7%)	1.000
Family history of CRC (%)	3 (3.3%)	0 (0.0%)	3 (3.5%)	31 (3.9%)	0.987
History of appendectomy (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	16 (2.0%)	0.337
Weight loss (%)	64 (70.3%)	4 (66.7%)	60(70.6%)	519 (66.0%)	0.411
Extraintestinal involvement (%)	23 (25.3%)	2 (33.3%)	21 (24.7%)	111 (14.1%)	0.005
Arthropathy	4 (4.4%)	0 (0.0%)	4 (5.1%)	40 (5.1%)	0.973
Skin lesions	6 (6.6%)	0 (0.0%)	6 (7.1%)	25 (3.2%)	0.171
Oral ulcer	12 (13.2%)	1 (16.7%)	11 (12.9%)	43 (5.5%)	0.004
Ophthalmopathy	1 (1.1%)	0 (0.0%)	1 (1.2%)	4 (0.5%)	0.423
Thrombosis	7 (7.7%)	1 (16.7%)	6 (7.1%)	13 (1.7%)	0.001
PSC	1 (1.1%)	0 (0.0%)	1 (1.2%)	10 (1.3%)	1.000
Hemoglobin, g/L (mean \pm SD)	102.62 \pm 25.48	108.10 \pm 20.43	102.56 \pm 25.68	112.04 \pm 26.20	<0.001

CRP, mg/L (median, IQR)	10.35 (2.20, 45.34)	4.61 (2.57, 20.35)	12.49 (2.20, 51.65)	8.54 (1.96, 29.51)	0.322
ESR, mm/h (median, IQR)	22 (12, 49)	15 (7, 16)	23 (12, 51)	20 (9, 38)	0.168
Treatment until stricture or the end of follow-up (%)					
5-ASA	87 (95.6%)	6 (100.0%)	81 (95.3%)	778 (99.0%)	0.032
Systemic glucocorticoids	77 (84.6%)	5 (83.3%)	72 (84.7%)	585 (74.4%)	0.032
Immunomodulators	26 (28.6%)	2 (33.3%)	24 (28.2%)	196 (24.9%)	0.450
Biologics	21 (23.1%)	0 (0.0%)	21 (24.7%)	309 (39.3%)	<0.001
Clinical activity until surgery or the end of follow-up (%)					<0.001
Clinical remission	26 (28.6%)	2 (33.3%)	24 (28.2%)	371(47.2%)	
Mild activity	23 (25.3%)	3 (50.0%)	20 (23.5%)	219 (27.9%)	
Moderate activity	26 (28.6%)	1 (16.7%)	25 (29.4%)	123 (15.6%)	
Severe activity	16 (17.6%)	0 (0.0%)	16 (18.8%)	73 (9.3%)	
Steroid dependence (%)	23 (25.3%)	0 (0.0%)	23 (27.1%)	123 (15.6%)	0.020
Steroid resistance (%)	6 (6.6%)	0 (0.0%)	6 (7.1%)	18 (2.3%)	0.041

UC-related surgery (%)	39 (42.9%)	6 (100.0%)	33 (38.8%)	71 (9.0%)	<0.001
CRC (%)	6 (6.6%)	-	-	16 (2.0%)	0.023
Severe intestinal complications (%)	27 (29.7%)	3 (50.0%)	24 (28.2%)	40 (5.1%)	<0.001
Bleeding	7 (7.7%)	0 (0.0%)	7 (8.2%)	26 (3.3%)	0.073
Perforation	3 (3.3%)	1 (16.7%)	2 (2.4%)	5 (0.6%)	0.041
Obstruction	15 (16.5%)	1 (16.7%)	14 (16.5%)	5 (0.6%)	<0.001
Fistula	3 (3.3%)	1 (16.7%)	2 (2.4%)	4 (0.4%)	0.017
Toxic megacolon	2 (2.2%)	0 (0.0%)	2 (2.4%)	1 (0.1%)	0.030
All-cause mortality (%)	3 (3.3%)	1 (16.7%)	2 (2.4%)	15 (1.9%)	0.621

¹Statistical comparisons were conducted between stricture and non-stricture groups.

IQR: interquartile range; IBD: inflammatory bowel disease; CRC: colorectal cancer; PSC: primary sclerosing cholangitis; SD: standard deviation; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; UC: ulcerative colitis.

Supplementary Table 8 Multivariate Cox regression analysis of risk factors for colorectal stricture formation in UC (excluding referred surgical cases and patients undergoing surgery within 30 days of diagnosis)

Variables	Univariate	Multivariate
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	HR (95% CI)	P value	HR (95% CI)	P value
Male	0.896 (0.621-1.293)	0.557		
Age at diagnosis \geq 40 yr	2.273 (1.562-3.308)	<0.001	2.150 (1.383-3.342)	<0.001
Montreal classification		0.079		0.319
E1 (proctitis)	1		1	
E2 (left-sided colitis)	0.555 (0.319-0.963)	0.036	0.611 (0.316-1.182)	0.143
E3 (pancolitis)	0.846 (0.525-1.362)	0.491	0.820 (0.464-1.451)	0.496
Extraintestinal involvement	2.077 (1.346-3.205)	<0.001	2.068 (1.270-3.368)	0.003
Hemoglobin	0.986 (0.979-0.992)	<0.001	0.985 (0.976-0.993)	<0.001
CRP	1.007 (1.002-1.011)	0.003	1.008 (1.002-1.015)	0.010
ESR	1.008 (1.001-1.015)	0.028	0.993 (0.982-1.004)	0.188
Treatment until stricture or the end of follow-up				
5-ASA	0.406 (0.163-1.012)	0.053	0.169 (0.053-0.534)	0.002
Systemic glucocorticoids	1.895 (1.145-3.135)	0.013	2.416 (1.262-4.624)	0.008
Immunomodulators	0.985 (0.654-1.482)	0.942		
Anti-TNF- α	0.764 (0.450-1.298)	0.320	0.753 (0.394-1.438)	0.390

VDZ	0.370 (0.199-0.689)	0.002	0.480 (0.251-0.918)	0.026
UST	0.049 (0.0-5887.28)	0.614	0.000(0.0-1.6E+164)	0.961

HR: hazard ratio; CI: confidence interval; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; 5-ASA: 5-aminosalicylic; anti-TNF- α : anti-tumor necrosis factor α ; VDZ: vedolizumab; UST: Ustekinumab.