



Supplementary Figure 1. Association of age at last visit with disease duration and age at diagnosis. (A) Association between age at last visit and disease duration. *X-axis* represents age at last visit and *Y-axis* represents disease duration. *P* value for association was calculated by linear regression without any covariates. *Blue line* represents regression line and *shaded area* represents 95% confidence. (B) Association between age at last visit and age at diagnosis. The form of figure is the same as described in (A).

Supplementary Table 1.List of Candidate Thromboembolic Disease-Related Genes

Gene	Associated disease
<i>F5</i>	Factor V Leiden
<i>F2</i>	Prothrombin mutation
<i>PROC</i>	Protein C deficiency
<i>PROS1</i>	Protein S deficiency
<i>SERPINC1</i>	Antithrombin III deficiency
<i>THBD</i>	Defect in thrombomodulin
<i>ADAMTS13</i>	Thrombotic thrombocytopenic purpura
<i>MTR</i>	Elevated homocysteine
<i>APOA</i>	Elevated lipoprotein(a)
<i>FGA, FGB, FGG</i>	Congenital dysfibrinogenemia
<i>F8</i>	Elevated factor VIII
<i>HRG</i>	Thrombophilia due to both elevated and deficient histidine-rich glycoprotein
<i>KNG1</i>	High-molecular-weight kininogen deficiency

Supplementary Table 2.Thrombophilia Pathogenic Variants Identified in Our Whole-Exome Sequencing Cohort

CHR	POS ^a	REF	ALT	Genes	Definition in CLINVAR ^b	Related disease in CLINVAR	No. of IBD subjects (total)	No. of IBD subjects with TED
1	169519049	T	C	<i>F5</i>	Drug response	Hormonal contraceptives for systemic use response, toxicity	37	5
1	169524537	C	G	<i>F5</i>	Pathogenic	Thrombophilia due to activated protein C resistance	2	1
1	173883881	G	A	<i>SERPINC1</i>	Pathogenic	Reduced antithrombin III activity/antithrombin deficiency	1	1
9	136291338	G	C	<i>ADAMTS13</i>	Likely pathogenic	Upshaw-Schulman syndrome	1	0
9	136302010	C	T	<i>ADAMTS13</i>	Likely pathogenic	Upshaw-Schulman syndrome	1	1
11	46747447	G	A	<i>F2</i>	Pathogenic	Prothrombin type 3	3	2
11	46761055	G	A	<i>F2</i>	Pathogenic	Venous thrombosis	40	3

ALT, alternative allele; CHR, chromosome; POS, position; REF, reference allele.

^aChromosomal positions are based on the Genome Reference Consortium human build 37 (GRCh37).

^bDefinition in CLINVAR is based on ftp://ftp.ncbi.nlm.nih.gov/pub/clinvar/vcf_GRCh37/archive_2.0/2019/clinvar_20190722.vcf.

Supplementary Table 3. Distribution of Thromboembolic Disease Polygenic Risk Score and Frequency of 2 major Thrombophilia Pathogenic Variants Among Patients With Inflammatory Bowel Disease and Controls

Variable	Control	IBD	<i>P</i> value ^a	β	SE
TED PRS, mean \pm SD	-0.054 \pm 0.999	0.015 \pm 1	.835	.0048	0.0229
Factor V Leiden, %	2.747	2.287	.258	-.1144	0.1012
Prothrombin (<i>F2</i>) G20210A mutation, %	1.464	1.917	.937	-.0105	0.1329

^a*P* values were calculated by logistic regression with 2 principal components.

Supplementary Table 4. Multivariate Analysis of Thromboembolic Disease History for Age at Last Visit, History of Inflammatory Bowel Disease Bowel Surgery, and Genetic Risk With Variance Inflation Factor^a

Variable	<i>P</i> value	OR	95% CI	VIF
Results with genetic risk				
Genetic risk (high) ^b	.0035	2.51	1.35–4.65	1.01
History of IBD bowel surgery	.0201	2.08	1.12–3.87	1.03
Age at last visit	.00003	1.04	1.02–1.05	1.03
Results with separated genetic risk (TPV and PRS)				
PRS (high) ^c	.0070	3.13	1.37–7.18	1.01
TPV carrier ^d	.0433	2.11	1.02–4.34	1.01
History of IBD bowel surgery	.0241	2.04	1.10–3.79	1.03
Age at last visit	.00002	1.04	1.02–1.06	1.03

CI, confidence interval; VIF, variance inflation factor.

^a*P* values, ORs, and VIFs were calculated by logistic regression with 2 principal components.

^bGenetic risk (high) is defined as having a high TED polygenic risk score (more than the top 5% of the control population distribution) or carried at least 1 TPV.

^cPRS (high) is defined as more than the top 5% of the control population distribution of TED PRS.

^dTPV carrier is defined as having at least 1 TPV.

Supplementary Table 5. Multivariate Analysis of Thromboembolic Disease History for Time-Dependent Parameters, History of Inflammatory Bowel Disease Bowel Surgery and Genetic Risk With Variance Inflation Factor^a

Variable	<i>P</i> value	OR	95% CI	VIF
Results with all time-dependent parameters (disease duration, age at diagnosis, and age at last visit)				
Genetic risk (high) ^b	.0035	2.52	1.35–4.68	1.01
History of IBD bowel surgery	.0159	2.18	1.16–4.09	1.06
Disease duration	.6043	0.98	0.90–1.06	13.65
Age at diagnosis	.7444	0.99	0.91–1.07	17.11
Age at last visit	.2227	1.06	0.97–1.15	26.50
Results with 2 time-dependent parameters (disease duration and age at last visit)				
Genetic risk (high) ^b	.0034	2.53	1.36–4.70	1.01
History of IBD bowel surgery	.0152	2.18	1.16–4.11	1.06
Disease duration	.4774	0.99	0.97–1.02	1.63
Age at last visit	.0001	1.04	1.02–1.06	1.57
Results with 2 time-dependent parameters (age at diagnosis and age at last visit)				
Genetic risk (high) ^b	.0034	2.52	1.36–4.69	1.01
History of IBD bowel surgery	.0164	2.17	1.15–4.07	1.06
Age at diagnosis	.5560	1.01	0.98–1.03	2.04
Age at last visit	.0065	1.03	1.01–1.06	2.10

CI, confidence interval; VIF, variance inflation factor.

^a*P* values, ORs, and VIFs were calculated by logistic regression with 2 principal components.

^bGenetic risk (high) is defined as having a high TED polygenic risk score (more than the top 5% of the control population distribution) or carried at least 1 TPV.

Supplementary Table 6. Association Between the Presence of Thrombophilia Pathogenic Variants and Polygenic Risk Score and History of Inflammatory Bowel Disease–Related Surgery and Extensive Disease^a

Variable	Presence of TPVs, n (%)		P value	OR (95% CI)
	Carrier ^b	Noncarrier		
History of IBD-related surgery	43 (59.72)	380 (59.10)	.91	1.03 (0.62–1.69)
Extensive disease (E3 or L3)	54 (75.00)	443 (68.90)	.18	1.52 (0.82–2.82)
Variable	PRS, n (%)		P value	OR (95% CI)
	High ^c	Low		
History of IBD-related surgery	26 (59.09)	397 (59.17)	.92	0.97 (0.52–1.81)
Extensive disease (E3 or L3)	29 (65.91)	468 (69.75)	.27	0.70 (0.36–1.33)

CI, confidence interval.

^aP values and ORs were calculated by logistic regression with 2 principal components.

^bTPV carrier is defined as having at least 1 TPV.

^cPRS high is defined as more than the top 5% of the control population distribution of TED PRS.