Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 86206

Title: Risk assessment of venous thromboembolism in inflammatory bowel disease by inherited risk in a population-based incident cohort

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02446417
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Doctor, Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: United States

Manuscript submission date: 2023-06-05
Reviewer chosen by: Geng-Long Liu
Reviewer accepted review: 2023-07-06 14:21
Reviewer performed review: 2023-07-14 08:47
Review time: 7 Days and 18 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In a population-based study of genetic risk stratification for VTE by F5/F2 and non-F2F5PGS in a large number of IBD patients, the finding that PGSnonF5/F2 is particularly useful is of interest. 1. The results showed that VTE was similar to that in cancer-bearing patients and developed over time. Previous reports have identified disease activity, hospitalization, and surgery as risk factors for the development of VTE. Please discuss whether the results are consistent with previous reports. 2. In Figure 1, the legends of Figs 1.c and d do not seem listed. Please fill in the contents of Fig1a-d in Result. 3. The top 10 quantile of PGSnonF5/F2 was more useful as a risk assessment method than F5/F2. Is it possible to develop a kit for clinical testing in the future? 4. Discuss prophylaxis in genetically high-risk cases of VTE.

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 86206

Title: Risk assessment of venous thromboembolism in inflammatory bowel disease by inherited risk in a population-based incident cohort

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05205091
Position: Peer Reviewer
Academic degree: MBBS
Professional title: Assistant Professor, Doctor, Staff Physician
Reviewer's Country/Territory: Singapore
Author's Country/Territory: United States

Manuscript submission date: 2023-06-05
Reviewer chosen by: Geng-Long Liu
Reviewer accepted review: 2023-07-23 15:52
Reviewer performed review: 2023-08-05 04:51
Review time: 12 Days and 12 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Scientific significance of the conclusion in this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors Rifkin and colleagues have generated rather interesting and novel data emphasising the relative importance of polygenic genetic risk assessment for thromboembolic events in IBD. The study has been very well-written and the data presented in a concise fashion. While the premise of the study is similar to Takeo Naito et al (also quoted as reference 24)'s earlier publication in Gastroenterology 2020, this current study utilises genotyping scoring data from a much larger cohort of thromboembolic cases and validates its scoring model in a very large IBD cohort (8300 patients) extracted from a biobank. Secondly, the authors were able to demonstrate polygenic risk scoring was superior to monogenic risk screening (F5/F2) in risk stratifying the cohort, with a distinct risk difference between the top and bottom deciles of PGS. It is well established that there are limitations in F5 and F2 monogenic mutation risk screening alone : the authors have alluded to this as well, and demonstrated this clearly in their data. The authors have mentioned the effects of ancestry and ethnicity briefly in their discussion - it could be discussed in greater detail by the authors that F5/F2 mutations are exceedingly rare in certain populations eg Asian

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

and African populations, and this begets the question whether their polygenic risk screening model would be even more discerning over monogenic (F5/F2)screening in other non-Caucasian populations. I agree with the authors' statement in their discussion that "additional data for non-European IBD patients is urgently needed" in this regard.

As this study was derived from data extraction off a biobank, it is perfectly understandable that major clinical and disease-specific variables (eg disease activity scores, medication use , biologic use,) would not be available for co-analysis. Yet, it has been quite well known IBD disease activity and perhaps medication use eg steroids , have major roles in modulating thromboembolic risk, and it is not clear if these polygenic risk models would be able to better enhance risk-stratification for VTE in these already high-risk patients. While the authors have acknowledged these limitations in their discussion, I would suggest the authors propose a clinical risk-stratification strategy utilising their proposed PGS scoring. As the authors pointed out, at least compared to cancer patients, IBD patients have a protracted risk of thromboembolic events long after hospital discharge. How do the authors propose using their PGS scoring to risk stratify which patients may require extended-duration thromboembolic prophylaxis for instance ? In addition, there are already clinical risk scores available for VTE risk - could the authors briefly propose how their PGS scoring could complement these clinical scores ? For instance , if a patient is already deemed high risk for a VTE based on clinical factors, would the PGS scoring influence perhaps choice of drug (steroids vs steroid-sparing agent , type/choice/duration of thromboembolic prophylaxis?)