World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2024 March 7; 30(9): 1250-1252

DOI: 10.3748/wjg.v30.i9.1250

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LETTER TO THE EDITOR

Genetic risk stratification of inflammatory bowel disease-associated venous thromboembolism: An Asian perspective

James Guoxian Huang

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Nikolić M, Croatia

Received: November 11, 2023
Peer-review started: November 11, 2023
First decision: January 5, 2024
Revised: January 8, 2024
Accepted: February 5, 2024
Article in press: February 5, 2024
Published online: March 7, 2024

James Guoxian Huang, Division of Gastroenterology, Hepatology and Nutrition, Department of Paediatrics, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore 119228, Singapore

James Guoxian Huang, Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 119228, Singapore

Corresponding author: James Guoxian Huang, MBBS, MRCP, Assistant Professor, Doctor, Division of Gastroenterology, Hepatology and Nutrition, Department of Paediatrics, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, NUHS Tower Block Level 12, 1E Kent Ridge Road, Singapore 119228, Singapore.
paehgj@nus.edu.sg

Abstract

The utilisation of polygenic scoring models may enhance the clinician's ability to risk stratify an inflammatory bowel disease patient's individual risk for venous thromboembolism (VTE) and guide the appropriate usage of VTE thromboprophylaxis, yet there is a need to validate such models in ethnically diverse populations.

Key Words: Thromboembolism; Inflammatory bowel disease; Genetic screening; Venous thromboembolism; Thromboprophylaxis

Core Tip: Polygenic scoring models may determine an inflammatory bowel disease patient's actual risk for venous thromboembolism (VTE) with greater accuracy than monogenic screening alone. This may be due to the cumulative effect of multiple prothrombotic genetic loci having a greater influence on thrombotic risk, rather than specific genetic mutations. There needs to be cross-validation of such scoring models in ethnically diverse populations as there is significant heterogeneity in the prevalence of genes implicated in thrombophilia. A composite score combining clinical and polygenic risk factors would further enhance the accuracy in determining one's VTE risk.

Citation: Huang JG. Genetic risk stratification of inflammatory bowel disease-associated venous thromboembolism: An Asian perspective. *World J Gastroenterol* 2024; 30(9): 1250-1252
URL: https://www.wjgnet.com/1007-9327/full/v30/i9/1250.htm
DOI: https://dx.doi.org/10.3748/wjg.v30.i9.1250

TO THE EDITOR

I read with interest a cohort study recently published by Rifkin *et al*[1] on the utility of genetic scoring models in the risk stratification for venous thromboembolism (VTE) in inflammatory bowel disease (IBD) patients. The premise of the study is similar to an earlier publication by Naito *et al*[2], in which the latter demonstrates the added value of polygenic genotyping to monogenic sequencing alone in determining VTE risk in a fairly large cohort of 792 IBD patients.

This current study, however, utilises genotyping scoring data from a much larger cohort of VTE cases and validates its scoring model in a large IBD cohort (n = 8300) extracted from a biobank. The authors had intentionally analysed a modified polygenic scoring model (PGS) that excluded the genetic contributions of the two mutations (F5: Factor V Leiden, F2: G20210A prothrombin gene mutation). Hence, they were able to demonstrate the clear superiority of polygenic risk scoring to monogenic risk screening in discriminating actual risk of VTE. Patients at the lowest decile of PGS had a far lower incidence of VTE (1.58%) than non-mutation carriers (4.31%). Interestingly, there was only a modest increment in discriminatory ability once the monogenic mutations of F5/F2 were re-added back into the PGS model.

The data suggests that an individual's genetic risk for VTE may be influenced to a greater extent by the cumulative effects of multiple pro-thrombotic genetic loci, rather than specific mutations alone. A multitude of clinical factors, such as ethnicity, comorbidities, IBD extent and activity, hypoproteinemic state, physical immobility, steroid use *etc.*, further add to the complexity in determining one's VTE risk in IBD. I agree with the authors' statement that additional data for non-European IBD patients is urgently needed, as previous publications do show commonly screened genetic mutations such as F5/F2 have a far smaller contributory role to VTE risk in other ethnic populations *e.g.* Asians and Africans[3-6]. This may also have implications in the standard diagnostic workup for thrombophilia in the non-European patient– it is possible a polygenic screening strategy may be more informative than monogenic testing. The authors also acknowledge that they did not analyse for other common mutations in anti-thrombin III protein (SERPINC1), protein C (PROC) and protein S (PROS1) given the relative rarity of such mutations. I would like to highlight that these mutations are relatively common in the Asian population compared to F5/F2 mutations, with a recent meta-analysis by Zhu *et al*[7] demonstrating the prevalence of PROC, PROS1 and SERPINC1 deficiency at 7.1%, 8.3% and 3.8% respectively in East Asian patients with VTE. This reiterates the need to validate the PGS model in other ethnic populations, as well as its performance against regionally prevalent thrombophilia mutations.

Precision medicine and personalised therapy remain as lofty targets at least in the current realm of IBD care, but the utilisation of a personalised, regionally validated risk scoring model would provide IBD clinicians invaluable guidance and confidence in the initiation of pharmacological thromboprophylaxis. Current adherence rates to thromboprophylaxis in hospitalised IBD patients remain low in spite of existing guidelines and the potential morbidity from IBD-associated VTE[8]. A composite score combining clinical and polygenic risk factors for VTE can identify the IBD patient at highest risk, justifying the continued use of thromboprophylaxis beyond hospitalisation for instance[9]. An objective assessment of VTE risk would also personalise therapeutic decisions pertaining to IBD control itself, with a greater impetus to consciously utilise steroid-sparing strategies in high-risk patients[10].

FOOTNOTES

Author contributions: Huang JG wrote the letter; and Huang JG revised the letter.

Conflict-of-interest statement: All the Authors have no conflict of interest related to the manuscript.

Country/Territory of origin: Singapore

ORCID number: James Guoxian Huang 0000-0002-5869-4194.

S-Editor: Qu XL
L-Editor: A
P-Editor: Qu XL

REFERENCES

1 **Rifkin AS**, Shi Z, Wei J, Zheng SL, Helfand BT, Cordova JS, Biank VF, Tafur AJ, Khan O, Xu J. Risk assessment of venous thromboembolism in inflammatory bowel disease by inherited risk in a population-based incident cohort. *World J Gastroenterol* 2023; **29**: 5494-5502 [PMID: 37900992 DOI: 10.3748/wjg.v29.i39.5494]

2 **Naito T**, Botwin GJ, Haritunians T, Li D, Yang S, Khrom M, Braun J; NIDDK IBD Genetics Consortium, Abbou L, Mengesha E, Stevens C, Masamune A, Daly M, McGovern DPB. Prevalence and Effect of Genetic Risk of Thromboembolic Disease in Inflammatory Bowel Disease. *Gastroenterology* 2021; **160**: 771-780.e4 [PMID: 33098885 DOI: 10.1053/j.gastro.2020.10.019]

3 **De Stefano V**, Chiusolo P, Paciaroni K, Leone G. Epidemiology of factor V Leiden: clinical implications. *Semin Thromb Hemost* 1998; **24**: 367-379 [PMID: 9763354 DOI: 10.1055/s-2007-996025]

4 **Gregg JP**, Yamane AJ, Grody WW. Prevalence of the factor V-Leiden mutation in four distinct American ethnic populations. *Am J Med Genet* 1997; **73**: 334-336 [PMID: 9415695 DOI: 10.1002/(sici)1096-8628(19971219)73:3<334::aid-ajmg20>3.0.co;2-j]

5 **Biswas A**, Bajaj J, Ranjan R, Meena A, Akhter MS, Yadav BK, Sharma V, Saxena R. Factor V Leiden: is it the chief contributor to activated protein C resistance in Asian-Indian patients with deep vein thrombosis? *Clin Chim Acta* 2008; **392**: 21-24 [PMID: 18342013 DOI: 10.1016/j.cca.2008.02.018]

6 **Qi X**, Wu F, Ren W, He C, Yin Z, Niu J, Bai M, Yang Z, Wu K, Fan D, Han G. Thrombotic risk factors in Chinese Budd-Chiari syndrome patients. An observational study with a systematic review of the literature. *Thromb Haemost* 2013; **109**: 878-884 [PMID: 23447059 DOI: 10.1160/TH12-10-0784]

7 **Zhu XJ**, Liu ZY, Wang PW, Wang J, Wen SD, Zhang JX, Zhu YJ, Sun ML, Xu XQ, Sun K, Lian TY, Cheng CY, Jing ZC. Congenital thrombophilia in East-Asian venous thromboembolism population: a systematic review and meta-analysis. *Res Pract Thromb Haemost* 2023; **7**: 102157 [PMID: 37674867 DOI: 10.1016/j.rpth.2023.102157]

8 **Levartovsky A**, Barash Y, Ben-Horin S, Ungar B, Klang E, Soffer S, Kopylov U. Thromboprophylaxis for Hospitalized Patients with Inflammatory Bowel Disease-Are We There Yet? *J Clin Med* 2020; **9** [PMID: 32858826 DOI: 10.3390/jcm9092753]

9 **Faye AS**, Wen T, Ananthakrishnan AN, Lichtiger S, Kaplan GG, Friedman AM, Lawlor G, Wright JD, Attenello FJ, Mack WJ, Lebwohl B. Acute Venous Thromboembolism Risk Highest Within 60 Days After Discharge From the Hospital in Patients With Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol* 2020; **18**: 1133-1141.e3 [PMID: 31336196 DOI: 10.1016/j.cgh.2019.07.028]

10 **Olivera PA**, Zuily S, Kotze PG, Regnault V, Al Awadhi S, Bossuyt P, Gearry RB, Ghosh S, Kobayashi T, Lacolley P, Louis E, Magro F, Ng SC, Papa A, Raine T, Teixeira FV, Rubin DT, Danese S, Peyrin-Biroulet L. International consensus on the prevention of venous and arterial thrombotic events in patients with inflammatory bowel disease. *Nat Rev Gastroenterol Hepatol* 2021; **18**: 857-873 [PMID: 34453143 DOI: 10.1038/s41575-021-00492-8]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com