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EDITORIAL COMMENT

What Are Your Expectations for Risk Prediction Tools?*

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The evolution of percutaneous coronary intervention (PCI) over the past few decades has significantly improved clinical outcomes in patients with ischemic heart disease. Although improvements in stent technology in the interventional field have remarkably reduced the incidence of stent thrombosis, bleeding events after PCI have recently drawn interventionalist attention.[1] A study from the TRACER (Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome) trial showed that not only myocardial infarction but also bleeding events significantly affected subsequent mortality and with similar time dependency.[2]

In this issue of *JACC: Asia*, Ng et al[3] report the incidence of bleeding events from a large-scale Chinese cohort (N = 33,570). Given that East Asians have different thrombotic and bleeding profiles from White patients, with higher vulnerability to bleeding and lower susceptibility to ischemic events (the East Asian paradox),[4] the investigators are to be commended for providing the largest scale evidence from real-world PCI findings in Asians to date. The estimated incidence rate of major bleeding after PCI was 5.74%, confirming a relatively high bleeding risk in this East Asian cohort and the necessity of developing an Asian-specific risk prediction model. To this end, the investigators developed a new bleeding risk assessment score, CARDIAC (anti-Coagulation therapy, Age, Renal insufficiency, Drop In hemoglobin, baseline Anemia in Chinese patients) score, for the prediction of International Society on Thrombosis and Haemostasis major bleeding from hospital discharge to 1 year. The score showed good discriminative performance (areas under the curve: 0.76 in the derivation cohort and 0.74 in the validation cohort) and predictive performance. Considering the East Asian paradox, the establishment of this Asian-specific risk prediction model is a significant contribution to this field.

Several risk prediction models to predict the risk for bleeding events and optimize antiplatelet therapy following PCI have been developed (**Table 1**). The PRECISE-DAPT (Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy) score (age, creatinine clearance, hemoglobin, white blood cell count, and previous spontaneous bleeding) showed potential in identifying patients at high bleeding risk (score ≥ 25) who might benefit from shortened (<12-month) dual-antiplatelet therapy (DAPT).[5] Patients not at high bleeding risk (score <25) might receive standard or prolonged (≥12-month) treatment without exposure to significant bleeding liability. The ADAPT score was created from the Grand-DES registry, consisting of patients treated with second-generation drug-eluting stents (N = 13,172).[6] The ischemic ADAPT score includes previous myocardial infarction or PCI, presentation as acute myocardial infarction, anemia, stent diameter <3 mm, and total stent length ≥30 mm, while the bleeding ADAPT score includes older age, low creatinine clearance, and anemia. Patients with net scores ≥1 had a higher ischemic than bleeding risk, while patients with net scores of −1 had higher bleeding than ischemic risk. Whereas the PRECISE-DAPT score and CARDIAC score evaluate bleeding risk only, the ADAPT score and CREDO-Kyoto risk score evaluate both bleeding and thrombotic risk.[7]

Several issues in this field remain unresolved. First, the weighted balance between bleeding and thrombotic events has yet to be investigated. Given

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TABLE 1 Bleeding Risk Assessment Tools for Patients Undergoing PCI

	DAPT Score[14]	PARIS Score[15]	PRECISE-DAPT Score[5]	BleeMACS Score[16]	CREDO-Kyoto Risk Score[7]	ADAPT Score[6]	CARDIAC Score[3]
Publication year	2016	2016	2017	2018	2018	2019	2022
Development cohort	DAPT randomized trial	PARIS registry	Pooled analysis of 8 randomized trials	BleeMACS registry	CREDO-Kyoto Registry Cohort-2	Grand DES registry	14 hospitals in Hong Kong
Patient number in the development cohort	11,648	4,190	14,963	15,401	4,778	13,172	16,785
Bleeding event	Major bleeding (12-30 mo after PCI)	Major bleeding at 2 y	Out-of-hospital bleeding at a median follow-up of 552 d	Serious spontaneous bleeding at 1 y	Major bleeding at 3 y	Major bleeding at a median of 1,126 d	Major bleeding at 1 y
Definition of bleeding	GUSTO moderate or severe	BARC type 3/5	TIMI major or minor	Protocol defined	GUSTO moderate or severe	TIMI major bleeding	ISTH major bleeding
C index (development cohort)	0.68	0.72	0.73	0.71	0.66	0.67	0.76
Validation cohort	PROTECT trial	ADAPT-DES registry	Bern PCI registry/PLATO trial	SWEDEHEART	RESET and NEXT trials	HOST-ASSURE and NIPPON trials	The original cohort was randomly split in a 1:1 ratio into development and validation cohorts
Patient number in the validation cohort	8,136	8,130	6,172/8,595	96,239 (ACS + PCI), 93,150 (ACS)	4,669	7,529	16,785
C index (validation cohort)	0.64	0.64	0.66/0.70	0.65 (ACS + PCI), 0.63 (ACS)	0.66	0.63	0.74
Thrombotic risk assessment	Yes	Yes	No	No	Yes	Yes	No

ACS = acute coronary syndrome; ADAPT-DES = Assessment of Dual Antiplatelet Therapy With Drug Eluting Stents; BARC = Bleeding Academic Research Consortium; BleeMACS = Bleeding Complications in a Multicenter Registry of Patients Discharged With Diagnosis of Acute Coronary Syndrome; C index = concordance index; DAPT = dual-antiplatelet therapy; GUSTO = Global Use of Strategies to Open Occluded Arteries; HOST-ASSURE = Harmonizing Optimal Strategy for Treatment of Coronary Artery Stenosis-Safety & Effectiveness of Drug-Eluting Stents & Anti-Platelet Regimen; ISTH = International Society on Thrombosis and Haemostasis; NIPPON = Nobori Dual Antiplatelet Therapy as Appropriate Duration; PARIS = Patterns of Non-Adherence to Anti-Platelet Regimen in Stented Patients; PCI = percutaneous coronary intervention; PLATO = Study of Platelet Inhibition and Patient Outcomes; SWEDEHEART = Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies; TIMI = Thrombolysis In Myocardial Infarction.

the overlap of bleeding and thrombotic risk factors, patients at high bleeding risk are also likely at high thrombotic risk.[8-11] The key is to consider the balance between bleeding and thrombotic risks. A further important viewpoint is to consider the severity of bleeding and thrombotic events: the differential impact of the various types of bleeding events on subsequent mortality risk is certainly known.[2] Although myocardial infarction had a greater impact than Bleeding Academic Research Consortium type 3a major bleeding (relative risk: 2.23; 95% CI: 1.36-3.64), it had less impact than Bleeding Academic Research Consortium type 3c major bleeding (relative risk: 0.22; 95% CI: 0.13-0.36). These different types of bleeding events have been lumped into the same category as major bleeding and simply compared with thrombotic events, but neither physicians nor patients ever treat these events equally. Assessment of the weighted balance between the 2 events is desirable and should be investigated in future studies. Second, the trade-off between practical utility and scientific accuracy also warrants consideration. Although web calculators are available for some of these prediction scores, getting physicians to take the time to calculate scores in real-world clinical practice would be challenging. A complicated tool would likely not be used, even in the face of high scientific accuracy. Our team has proposed a practical assessment method for the balance between bleeding and thrombotic risks using Academic Research Consortium for High Bleeding Risk criteria.[12] Finally, further fine-tuning of the score to adjust for the ultra-short DAPT era is warranted; those scores established so far were all derived from patients treated with relatively long DAPT duration. Some clinical trials are even evaluating a no-DAPT strategy.[13]

In summary, the study by Ng et al[3] is a welcome contribution to the published research, confirming the high bleeding risk of East Asian populations and providing a novel Asian-specific bleeding risk assessment tool. Nevertheless, several unsolved issues remain. What are your expectations for risk prediction tools: science or practical utility? Fair comparison between which bleeding and thrombotic events? We might wish to build a consensus around such points before further investigation to fine-tune the models.

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