

Risk Evaluation Tools for Prediction and Possible Guidance of DAPT: Is Scoring a Hit in East Asians Patients undergoing PCI?

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Thromb Haemost 2019;119:1033–1035.

The benefit of dual antiplatelet therapy (DAPT) in the acute and chronic phase after percutaneous coronary intervention (PCI) for acute coronary syndromes (ACSs) or stable coronary artery disease (SCAD) has been thoroughly validated in a large number of clinical trials.^{1,2} While potent ischemic event protection is essential in the acute phase after PCI but also thereafter, bleeding events are an accumulative issue during the maintenance phase. Counterbalancing hazards from stent thrombosis and recurrent myocardial infarction versus a pharmacologically aggravated bleeding disposition remains an ongoing challenge for the cardiologist.³ Not only the choice of drugs for DAPT and their dosage, but also the duration of DAPT is at discussion.^{1,4} Previous scientific statements on DAPT duration and intensity have summarized a multitude of factors affecting ischemic and bleeding risk after PCI for ACS or SCAD.^{4–6} Most notably, the DAPT,⁷ PRECISE-DAPT,⁸ and PARIS⁹ risk scores were introduced as valuable risk prediction tools integrating and correlating the ischemic benefit and bleeding risk for guidance of DAPT. However, the vast majority of clinical trials in the field of DAPT as well as the above-mentioned risk scores were evaluated in the Western population and study cohorts included little to no East Asian patients. In consequence, there is a large gap of knowledge for this patient population, including choice and dosage of drugs as well as dedicated scoring systems.

In this issue of *Thrombosis and Haemostasis*, Kang et al¹⁰ take efforts to establish a risk-adjusted dichotomous DAPT score, specifically adapted to East Asian patients undergoing PCI. Five different registries were pooled and data from 13,172 patients receiving second-generation drug-eluting stents (DESs) and clopidogrel treatment were used for this

important, innovative, and novel analysis. Of note, patients who received a first-generation DES were excluded from the analysis. Ischemic and bleeding endpoints were assessed up to 3 years after index PCI. A net *Asian dual antiplatelet treatment score (ADAPT score)* was derived by subtraction of an estimated bleeding score (B-ADAPT) from an estimated ischemic score (I-ADAPT). External validation was conducted in the HOST-ASSURE¹¹ and NIPPON¹² trials and a comparison of the discriminative ability between the ADAPT and the PARIS risk score models was presented.

Key findings of this study were that the discriminative power of both, the I-ADAPT (*c*-statistics 0.649, 95% confidence interval [CI], 0.610 – 0.688, *p* < 0.001, goodness of fit *p* = 0.898) and the B-ADAPT (*c*-statistics 0.664, 95% CI, 0.620 – 0.708, *p* < 0.001, goodness of fit *p* = 0.880) scores were moderate but significant—as was the discriminative performance of other previous score models.^{7–9} Further, best cut-off values were calculated for the I-ADAPT and B-ADAPT scores. Values above 3.0 were highly predictive of an increased ischemic and bleeding risk (1.0% vs. 2.3%, *p* < 0.001 for I-ADAPT, 0.9% vs. 2.8%, *p* < 0.001 for B-ADAPT). The net-ADAPT score was correlated with the net clinical risk and a higher ischemic risk compared with the bleeding risk was suggested when the score was ≥ 1 , whereas a higher bleeding risk compared with ischemic risk was suggested when the score was ≤ -1 . External validation of the ADAPT scores by the HOST-ASSURE and NIPPON cohorts showed reliable and consistent results compared with the derivation cohort. Of note, patient characteristics clearly reflect the overall lower body mass index in East Asian patients compared with Western populations and indicate a high rate (around one-third) of

received
May 7, 2019
accepted
May 7, 2019

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Stuttgart · New York

DOI <https://doi.org/10.1055/s-0039-1692169>.
ISSN 0340-6245.

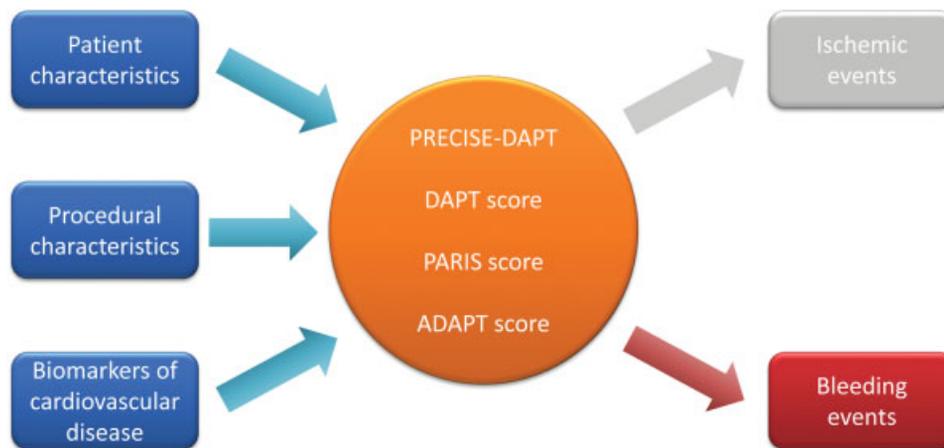


Fig. 1 Risk prediction after percutaneous coronary intervention (PCI) and score for possible guidance of antiplatelet treatment. Calculation of dual antiplatelet therapy (DAPT) risk scores by integrating patient characteristics, procedural variables, and biomarkers of cardiovascular disease. Risk scores may be capable of predicting both ischemic and bleeding events and PRECISE-DAPT and DAPT may be used for guidance of treatment according to current European Society of Cardiology (ESC) guidelines.^{1,5}

patients under DAPT after 3 years of follow-up. The authors conclude that their novel ADAPT scores predict ischemic and bleeding events in East Asian patients and that those scores could be used to determine DAPT duration.

Kang et al are to be commended for this study and for trying to establish a scoring system that could be unique for risk prediction and possible guidance of DAPT in the East Asian population. Besides a large sample size, the exclusive use of second-generation DES and integration of clinical and procedural variables is certainly a strength of the study along with a sound statistical processing. However, several limitations must be acknowledged when examining the data.

First, the risk prediction of the scoring systems under investigation was found to be significant but the discriminatory power of the models was only modest (as expected for clinical risk scores). Thus, while the ADAPT scores could be used for predicting ischemic and bleeding risk in East Asian patients, their role for a guidance of DAPT including determination of DAPT duration definitely requires the conduction of further dedicated clinical studies. At best, a randomized parallel-group clinical trial could be conducted that includes a fixed duration in the control arm (along with guideline recommendations) versus a determination of variable DAPT durations based on the ADAPT score in an experimental arm of such a study. Such data seems mandatory for providing robust evidence to include this specific scoring system into clinical routine practice.

Second, the overall bleeding risk is low in this cohort with major bleeds (classified according to the Thrombolysis In Myocardial Infarction [TIMI] definition) below 2%. This may also relate to the lack of data on ACS patients treated with the potent P2Y₁₂ adenosine diphosphate receptor blockers ticagrelor or prasugrel. In consequence, it remains unclear in how far these findings could be extrapolated to current clinical practice where treatment with potent antiplatelet drugs should be standard of care in ACS patients undergoing PCI. Further investigations are mandatory to test the pre-

dictive value of the ADAPT score in ACS patients receiving ticagrelor or prasugrel.

Finally, the bleeding complications captured in this study included major bleeds only and were defined according to the TIMI bleeding classification. For a more in-depth investigation on bleeding events and how they relate to the scoring systems, it seems mandatory to include minor bleeds as well and to possibly expand bleeding event classifications to modern definitions like the Bleeding Academic Research Consortium bleeding classification.¹³

In summary, bleeding and ischemic risk prediction in patients undergoing PCI is complex and this holds also true for the inclusion of scoring systems when trying to find the best predictors of patient's risk (→ Fig. 1). Bleeding risk is also a highly dynamic process, and its variation over time is often a better determinant of bleeding events; indeed, a bleeding score should help identify the modifiable bleeding risk factors and, subsequently, to facilitate the identification of "high-risk" subjects for more frequent review and follow-up.¹⁴ All prior risk scores including the DAPT and PRECISE-DAPT scores were not established in dedicated randomized trials but were designed and calculated in a post hoc fashion from the data of preceding clinical trials. This also explains the relatively "weak" class IIb ("may be considered") recommendations in current European guidelines^{1,5} for the use of scores for guidance of DAPT. For both Western and East Asian patients undergoing PCI with DAPT much more data are urgently needed before those scores could find their way into clinical routine. The study by Kang et al is a first and important step into this direction for a better and more individualized treatment of East Asian patients undergoing PCI.

Conflict of Interest

D.S. has received speaker fees and honoraria for consulting from Sanofi Aventis, Pfizer, Daiichi Sankyo, Bayer Vital, AstraZeneca, and Roche Diagnostics; and research grants from Roche Diagnostics. F.W.A.V. has received educational and research grants from Bayer Healthcare and

Boehringer Ingelheim; and has received honoraria for consultancies and/or presentations from Daiichi-Sankyo, BMS/Pfizer, Boehringer Ingelheim, and Bayer Healthcare. R.H. has reported that he has no relationships relevant to the contents of this paper to disclose.

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