

Editorial



High-Bleeding-Risk Criteria as a Modifier of Treatment Effect During Antithrombotic Therapy

Phil Iver Guevarra , MD^{1,2}, Sang-Wook Kim , MD, PhD^{1,3}, and Young-Hoon Jeong , MD, PhD^{3,4}

¹Heart and Brain Hospital, Chung-Ang University Gwangmyeong Center, Gwangmyeong, Korea

²Silang Specialist Medical Center, Silang, Cavite, Philippines

³Division of Cardiology, Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea

⁴CAU Thrombosis and Biomarker Center, Chung-Ang University Gwangmyeong Hospital, Gwangmyeong, Korea

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Correspondence to

Young-Hoon Jeong, MD, PhD

CAU Thrombosis and Biomarker Center,
 Chung-Ang University Gwangmyeong Hospital,
 110, Deokan-ro, Gwangmyeong 14353, Korea.

Email: gooddoctor@naver.com

younggooddoctor@gmail.com

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In patients with atherosclerotic cardiovascular disease, bleeding events pose a critical threat to long-term clinical outcomes during antithrombotic therapy. Achieving an optimal balance between thrombotic and bleeding risks has become increasingly challenging, as the factors contributing to both risks frequently coexist.¹⁾ To address this issue, bleeding-avoidance strategies—such as tailoring the duration, dose, or potency of antithrombotic regimens—have been developed to reduce serious bleeding complications, particularly in patients with a high bleeding risk (HBR) phenotype.

Dose adjustment of direct oral anticoagulants (DOACs) is widely practiced based on the underlying disease and patients' baseline characteristics.²⁾³⁾ In atrial fibrillation (AF), DOAC dosing is determined according to age (≥ 80 years), body weight (≤ 60 kg), and renal function (creatinine clearance [CrCl] < 50 mL/min) (Table 1).³⁻⁷⁾ In addition, current guidelines

Table 1. Key risk factors related with bleeding risk: Antiplatelet therapy vs. direct oral anticoagulant

Criteria	ANTIPLATELETS	DOACs
AGE	- Bleeding risk increases markedly in elderly patients ≥ 75 years: a minor criterion of ARC-HBR - Prasugrel: reduced dose of 5 mg if ≥ 75 years - Other antiplatelets: no formal dose-adjustment	- Bleeding risk increases markedly in elderly patients - Apixaban: dose-reduction if ≥ 80 years + additional risks - Dabigatran: dose-reduction if ≥ 80 years - Edoxaban and rivaroxaban: no formal dose-adjustment
WEIGHT	- Bleeding risk increased in low body weight < 55 kg (men), < 50 kg (women): a major criterion of J-HBR - Prasugrel: reduced dose of 5 mg if < 60 kg - Other antiplatelets: no formal dose-adjustment	- Bleeding risk increased in low body weight - Apixaban: dose-reduction if ≤ 60 kg + additional risks - Edoxaban: dose-reduction if ≤ 60 kg - Dabigatran and rivaroxaban: no formal dose-adjustment
KIDNEY FUNCTION	- Bleeding risk increases in renal failure - eGFR 30 to < 60 mL/min: a minor criterion of ARC-HBR - eGFR < 30 mL/min: a major criterion of ARC-HBR - Antiplatelets: no formal dose-adjustment	- Bleeding risk increases in renal failure - Apixaban: dose-reduction if creatinine ≥ 133 μmol/L + additional risks - Dabigatran, edoxaban and rivaroxaban: dose-reduction if CrCl 15 to < 50 mL/min

ARC-HBR = Academic Research Consortium for High Bleeding Risk; CrCl = creatinine clearance; eGFR = estimated glomerular function rate; J-HBR = Japanese criteria for High Bleeding Risk

Defining HBR Criteria

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ORCID iDs

Phil Iver Guevarra  <https://orcid.org/0009-0006-5470-3299>
Sang-Wook Kim  <https://orcid.org/0000-0002-7208-8596>
Young-Hoon Jeong  <https://orcid.org/0000-0003-0403-3726>

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Conflict of Interest

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Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions

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recommend using bleeding risk scores in AF patients.^{3,4)} Among these, the HAS-BLED score is the most widely used tool for estimating the risk of major bleeding in AF patients receiving oral anticoagulants. HAS-BLED is an acronym for Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly (age >65 years), and Drugs/alcohol. This score facilitates identification of patients with modifiable bleeding risk factors that can be addressed to potentially reduce bleeding risk.

In 2019, the Academic Research Consortium for High Bleeding Risk (ARC-HBR) proposed a consensus definition for identifying patients at HBR undergoing percutaneous coronary intervention (PCI), based on a review of available evidence (**Table 1**).⁵⁾ HBR was defined as a risk of Bleeding Academic Research Consortium (BARC) type 3 or 5 bleeding $\geq 4\%$ at 1 year, or a risk of intracranial hemorrhage (ICH) $\geq 1\%$ at 1 year. This HBR criteria comprise 14 major and 6 minor components: a major criterion, when present alone, is considered to confer a BARC 3 or 5 bleeding risk $\geq 4\%$ at 1 year or an ICH risk $\geq 1\%$ at 1 year. A minor criterion, when present alone, is considered to confer an increased bleeding risk, with a BARC 3 or 5 bleeding rate $<4\%$ at 1 year.

Similar to the dose-adjustment and bleeding risk assessment criteria applied during DOAC therapy,^{3,4)} the ARC-HBR criteria also incorporate modifiable bleeding risk factors in the context of antiplatelet therapy.⁵⁾ For example, moderate chronic kidney disease (CKD) (estimated glomerular filtration rate [eGFR] 30–<60 mL/min) is considered a minor criterion, whereas severe or end-stage CKD (eGFR <30 mL/min) is designated as a major criterion. In addition, the consensus defines age ≥ 75 years as a minor criterion; however, this HBR criteria do not include low body weight as a risk factor.⁶⁾

Multiple strategies modifying the intensity, duration, or both aspects of dual antiplatelet therapy (DAPT) have been investigated to mitigate bleeding risk without compromising ischemic protection.^{1,7)} The decision to abbreviate or de-escalate DAPT relies on individual clinical judgment, guided by the perceived balance between ischemic and bleeding risks, potential adverse events, comorbidities, concomitant medications, and the availability of the respective agents. An expert consensus recommends using HBR criteria (e.g., the ARC-HBR classification) to guide clinical judgment and decision-making when implementing this strategy.⁸⁾ However, the consensus also notes that if age is the only underlying factor, at least one additional risk factor should be present.

In this issue of the *Korean Circulation Journal*, Jin et al.⁹⁾ reported the clinical outcomes of short-term (1–6 months) versus standard (12 months) DAPT after drug-eluting stent implantation, including 10,487 patients from five contemporary Korean randomized trials, of whom 1,571 (15.0%) were aged ≥ 75 years. The authors conducted an age-stratified analysis to evaluate the consistency of the DAPT strategy effect across age groups. During the 1-year follow-up, these analyses revealed the increased risks of major bleeding and ischemic events across the patients aged <62 years, 62–74 years, and ≥ 75 years. In patients aged ≥ 75 years, the standard DAPT strategy was significantly associated with a higher risk of major bleeding compared to the short-term DAPT strategy (3.5% vs. 1.5%: hazard ratio [HR], 2.34; 95% confidence interval [CI], 1.17–4.68; $p=0.016$), while no significant difference was observed between the 2 treatment groups in patients aged <75 years (1.5% vs. 1.1%: HR, 1.45; 95% CI, 1.00–2.10; $p=0.053$). However, the clinical implication of this criterion should not be overinterpreted, given that the p for interaction was 0.207. The risks of ischemic events did not differ significantly between DAPT strategies and age groups. Although this study provides

important findings for clinical practice, several concerns remain. The included trials were not identified through a formal systematic review process. Moreover, as all trials were conducted exclusively in Korean cohorts, extrapolation of these results to other ethnic populations should be approached with caution.

A simplified assessment of the HBR phenotype is needed to facilitate the implementation of de-escalation or abbreviated strategies following PCI. Unlike the dose-adjustment criteria used for DOACs, the ARC-HBR criteria do not account for the prognostic implications of low body weight or body mass index. In 2020, the 'Japanese version of the HBR criteria'⁶⁾ expanded the ARC-HBR framework by incorporating additional variables, including low body weight (<55 kg for men, <50 kg for women), frailty (e.g., elderly women), CKD requiring dialysis, heart failure, and peripheral vascular disease (**Table 1**). The 2025 Updated Position Statement for East Asians¹⁰⁾ also emphasized low body weight as a key HBR determinant, particularly in East Asian patients—a finding that may further support the 'East Asian Paradox,' reflecting the higher bleeding risk in East Asians compared with Western populations.

If HBR can be assessed using simple parameters such as age and body weight, it could serve as a practical indicator in routine clinical care. The TRITON–TIMI 38 trial⁷⁾ already demonstrated that age and body weight were pivotal in determining the optimal prasugrel dosage: patients weighing <60 kg or aged ≥75 years were recommended a reduced 5 mg maintenance dose, whereas those weighing ≥60 kg and aged <75 years generally received the standard 10 mg dose.

Taken together, the HBR phenotype can be evaluated using the same covariates regardless of the antithrombotic regimen. Age and body weight (or body mass index) are easily obtained during treatment, and renal function assessment is closely related to these risk factors. However, the cutoffs for age and body weight, as well as the methods for evaluating renal function (e.g., CrCl vs. eGFR), vary across regimens and risk scoring systems. Standardizing these parameters would enable their consistent application for HBR assessment in daily practice.

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