

CLINICAL RECOMMENDATION

Position Statement on Antiplatelet Therapy for East Asians With Coronary Artery Disease

2025 Update



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ABSTRACT

Growing clinical evidence has indicated that East Asian patients have a lower risk for cardiovascular events but a higher risk of serious bleeding during antiplatelet therapy compared with Western populations—referred to as the “East Asian Paradox.” The unique risk-benefit tradeoff observed in East Asian populations has been a topic of interest, which may be influenced by a complex interplay of genetic and environmental risk factors—such as specific atherothrombotic cardiovascular risks, helicobacter pylori infection, and low body weight. There exist knowledge gaps in the antiplatelet therapy among East Asian populations with coronary artery disease, such as the individualized assessment of ischemic and bleeding risk, de-escalation strategy of dual antiplatelet therapy and the compliance of long-term secondary prevention. A substantial body of positive evidence supporting de-escalation strategies of dual antiplatelet therapy comes from East Asia, possibly caused by the distinct therapeutic range of antiplatelet effects and heightened pharmacodynamic response to potent P2Y₁₂ inhibitors observed in this population. This consensus update focuses on the latest progress and hotspot issues on antiplatelet therapy in the East Asian population with coronary artery disease and therapeutic recommendations based on the best available evidence. (JACC Asia. 2025;5:821-846) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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Shun Kosaka, MD, PhD, served as Guest Associate Editor for this paper. Toru Suzuki, MD, PhD, Associate Editor, served as the acting Editor-in-Chief and main adjudicator for this paper.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

CAD = coronary artery disease

CCS = chronic coronary syndrome

CV = cardiovascular

DAPT = dual antiplatelet therapy

DES = drug-eluting stent(s)

HBR = high bleeding risk

MACE = major adverse cardiovascular event

MI = myocardial infarction

NACE = net adverse cardiovascular event

PCI = percutaneous coronary intervention

Coronary artery disease (CAD) covers a continuous spectrum of diseases, and acute coronary syndrome (ACS) and chronic coronary syndrome (CCS) are different stages of CAD. According to the latest “Report on Global Burden of Disease,” incidence and mortality associated with CAD have varied significantly according to the region.¹ In 2019, there were 46.649 million prevalent cases of CAD in East Asia countries (traditional East Asian countries including China, Japan, South and North Korea, Mongolia, and so on), with an age-standardized rate of 2,312.7 per 100,000, which was 6.0% higher than that found in 1990. In 2019, age-standardized CAD death in East Asia was 114.3 per 100,000, which increased by 15.8% compared with 1990. In high-income North America and Western

Europe, the age-standardized prevalence of CAD in 2019 was 1,625.9 and 1,810.7 per 100,000, respectively, 36.2% and 17.3% lower than in 1990. Additionally, the age-standardized CAD death rates in 2019 were 88.1 per 100,000 in high-income North America and 60.7 per 100,000 in Western Europe, which decreased by 51.0% and 61.2% compared with 1990. These data indicate that while the prevalence and mortality of CAD have declined in high-income Western countries, they have increased in East Asia, highlighting a growing burden of CAD in that region.

In recent years, percutaneous coronary intervention (PCI) techniques have developed rapidly, becoming the primary treatment option for patients with high-risk CAD, particularly those presented with acute myocardial infarction (AMI). Antiplatelet therapy has been the cornerstone in CAD management, especially for ACS patients undergoing PCI.²⁻⁸ However, previous randomized controlled trials (RCTs) on guidelines of antiplatelet therapy have predominantly focused on the Western populations, despite notable differences in thrombosis and bleeding risks, as well as the therapeutic range of antiplatelet effect between East Asian and Western patients (Figure 1).⁹

In 2012, Jeong et al. introduced the comprehensive concept of the “East Asian Paradox,” describing how East Asian patients experience reduced anti-ischemic benefits and increased bleeding risk during antithrombotic therapies compared with

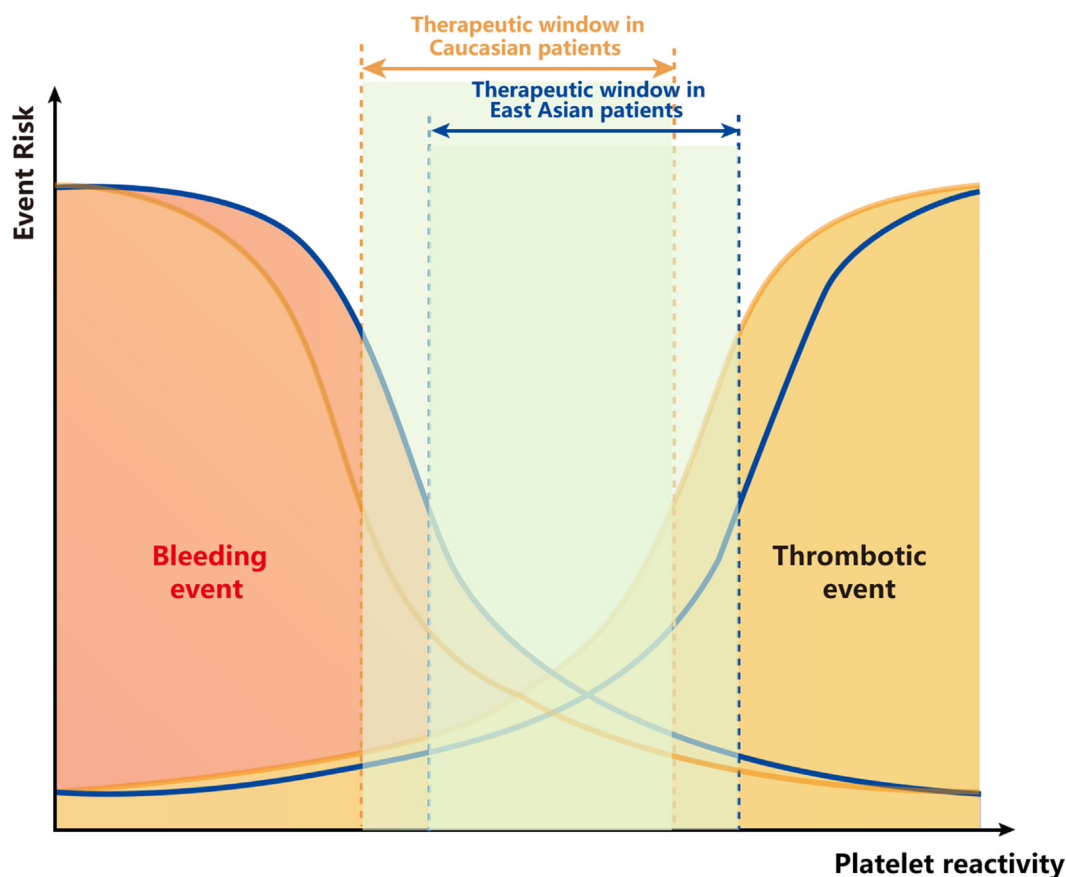
Caucasian patients,¹⁰ which has since been further supported by numerous contemporary clinical trials and reviews.^{11,12} In 2014, through a joint effort by the World Heart Federation and East Asian experts, the first edition of the “Expert Consensus Statement on Antiplatelet Therapy in East Asian patients with ACS or undergoing PCI”⁹ was published. This statement highlighted the unique balance of clinical efficacy and safety during antithrombotic therapy in the East Asian population, as well as the possibility of distinct benefits observed following the introduction of potent P2Y₁₂ inhibitors for ACS patients. The “2018 Update of Expert Consensus Statement on Antiplatelet Therapy in East Asian patients with ACS or undergoing PCI,”¹³ issued by the Asian Society of Cardiology, incorporated emerging new research evidence specific to the East Asian population. This update advocated for the further standardization of dual antiplatelet therapy (DAPT) for the East Asian population. A consensus¹⁴ and a paper covering 2 companion network meta-analyses,¹⁵ both published in 2023, were focused on the DAPT strategy in CAD, but these studies predominantly included clinical data from Western populations. A comprehensive literature search was conducted from July 2023 to December 2024. Clinical studies, systematic reviews and meta-analyses, and other evidence conducted on human participants were identified that were published in English from MEDLINE (through PubMed), EMBASE, the Cochrane Library, SinoMed, and other selected databases relevant to this consensus.

In recent years, novel clinical research from East Asian countries has explored various de-escalation strategies for DAPT and long-term antiplatelet therapy in CAD patients. Accordingly, this updated consensus will focus on the latest findings relevant to these patients. This updated consensus expands its focus to address antiplatelet therapy for CAD as a whole, rather than focusing solely on ACS or PCI as in the 2018 version, for East Asian patients. New recommendations are included for the “prediction and evaluation of bleeding and ischemic risks,” “antiplatelet therapy for CCS,” “antiplatelet therapy for special populations,” and “compliance of antiplatelet therapy.” In addition, the recommendations for “initial therapy, duration and de-escalation of DAPT for patients with ACS” have been updated.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors’ institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

Manuscript received April 15, 2024; revised manuscript received February 10, 2025, accepted April 1, 2025.

FIGURE 1 Different Therapeutic Antiplatelet Effect in East Asian vs Western Patients^{9,10}



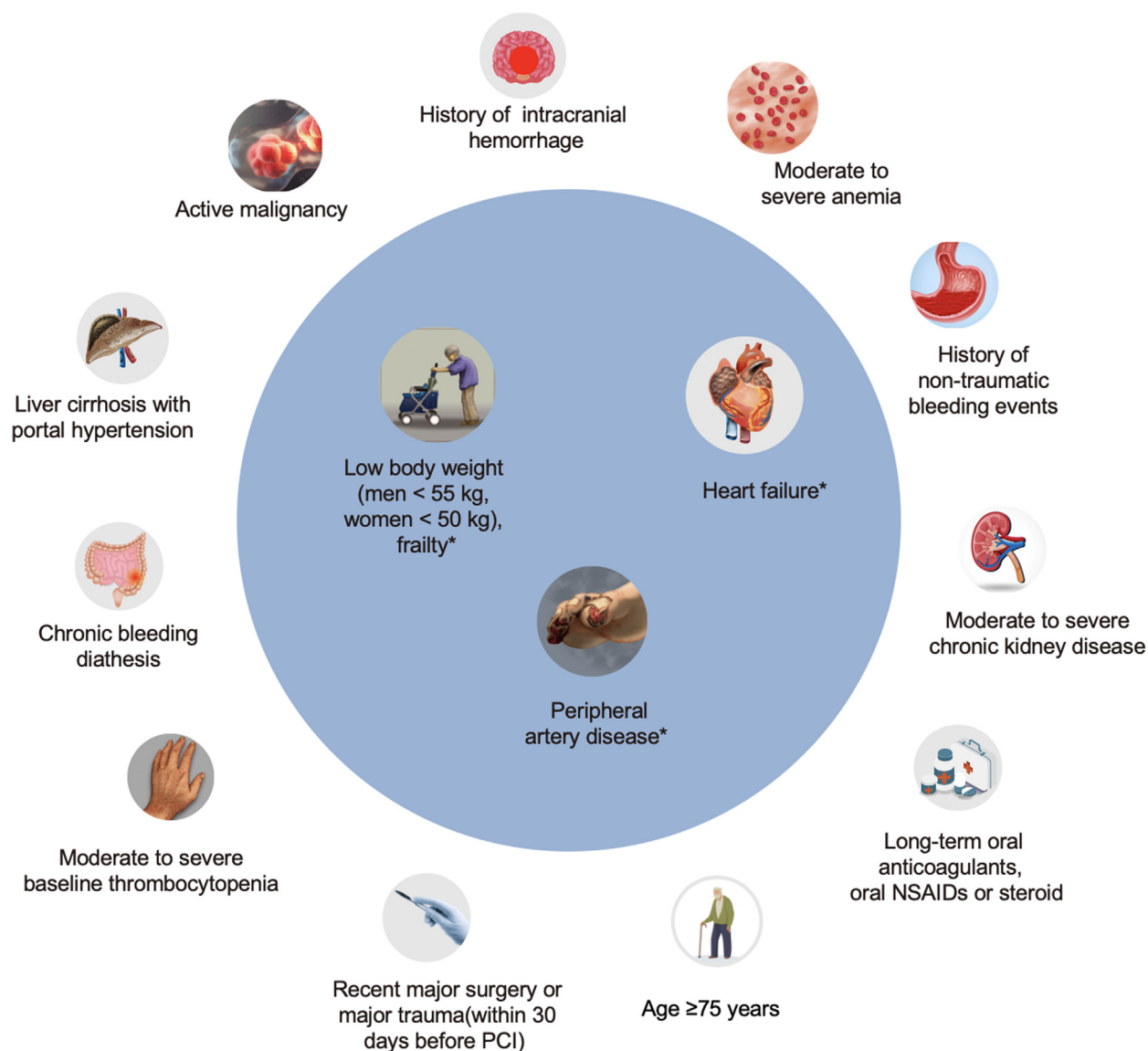
East Asian patients exhibit a lower risk of ischemic events compared with Western patients, which may be partly attributed to lower levels of atherothrombotic cardiovascular risks, such as inflammation and coagulation activity. Furthermore, East Asians have a heightened tendency for gastrointestinal and intracranial hemorrhage. Clinical evidence supports a unique balance between ischemic and bleeding risks in East Asian patients undergoing antiplatelet therapy, as reflected by different thresholds (eg, P2Y₁₂ reaction unit measured by VerifyNow test) for high- and low-platelet reactivity in this population.

PREDICTION AND EVALUATION OF BLEEDING AND ISCHEMIC RISKS IN EAST ASIANS

The East Asian population, with a notably higher risk of bleeding, has distinct ischemic and hemorrhagic profiles compared with the Western population,^{11,16} and intensive antiplatelet therapy has not provided further clinical benefit.¹⁷⁻¹⁹ The European Society of Cardiology (ESC) guidelines^{4-6,8} state that the intensity of antiplatelet therapy and the duration of DAPT should be determined through an initial assessment of bleeding risk. Therefore, how to identify and assess the bleeding and ischemia risks in East Asian patients with CAD is crucial for standardizing antiplatelet therapy management in this population.

HIGH BLEEDING RISKS IN EAST ASIANS. In 2019, the Academic Research Consortium for High Bleeding Risk (ARC-HBR) released the definition and criteria of high bleeding risk (HBR), including 14 major criteria and 6 minor criteria.¹⁶ Effectiveness of the ARC-HBR criteria was validated in patients from Japan, China, and South Korea.²⁰⁻²² However, this criterion appeared limited and less applicable in ACS patients, because it underestimated the risk of bleeding in those with fewer than 2 minor criteria or a single major criterion.²³ The risk factors for bleeding outlined by the ARC-HBR criteria in the pre-existing populations may be insufficient and the risk factors of these criteria should be broadened to better reflect the realistic risks of HBR patients, particularly within the East Asian population.

FIGURE 2 Factors for High Bleeding Risk in East Asian CAD Patients



***Factors in the inner circle are added to predict bleeding risk in East Asians**

*Risk factors suggested from the Japanese-HBR score.²⁴ DAPT = dual antiplatelet therapy; NSAID = nonsteroidal anti-inflammatory drug; PCI = percutaneous coronary intervention.

The 2020 Japanese Circulation Society guideline²⁴ suggested common characteristics—such as low body weight, frailty, heart failure, and peripheral artery disease (PAD)—not covered by the ARC-HBR criteria but identified as the important factors for HBR in the East Asian population. These risk factors were incorporated to develop the J-HBR criteria specifically tailored for the East Asian population. Especially, this criterion indicated the clinical significance of low

body weight (men <55 kg, and women <50 kg) in defining HBR phenotype, which can be a key risk factor contributing to the difference in bleeding risk between East Asian and Western populations. The incidence and effectiveness of the HBR phenotype defined by the J-HBR criteria were validated in large-scale registries including East Asians undergoing PCI, with incidence reaching up to ~60%.^{25,26} The 2020 Asian Pacific Society of Cardiology Consensus

Recommendations on Antithrombotic Management for High-risk Chronic Coronary Syndrome proposed the “age-bleeding-organ dysfunction” (ABO) algorithm to identify the populations with HBR among East Asian patients presented with CCS.²⁷ Based on the clinical evidence, the HBR standard for CAD patients in East Asia is shown in **Figure 2** and **Table 1**.

HIGH ISCHEMIC RISKS IN EAST ASIANS. According to the 2020 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-Segment Elevation, the clinical factors for assessing the risk of thrombotic events in CAD patients are summarized, and can be used as a reference for DAPT decision-making for East Asian patients.⁴ By combining ischemic risk scores in East Asia, such as Asian DAPT score, CREDO-Kyoto risk score, and KAMIR-DAPT score (**Supplemental Table 1**), the high ischemic risks in East Asia are shown in **Figure 3** and **Table 2**.

BLEEDING AND ISCHEMIA SCORING. Antithrombotic therapy in CAD patients requires a balance between ischemic and bleeding risks. A single risk factor is not enough to comprehensively determine the risk of bleeding or ischemic events. Some scoring tools can provide very valuable clues to the severity, risk, or prognosis of the disease, to assist the diagnosis and treatment of the disease. The common scoring systems include GRACE, CRUSADE, ACUTY, TIMI, PRECISE-DAPT, DAPT, and SYNTAX. Detailed information about these scoring systems was described in **Supplemental Materials 1 and 2**.

LIMITATIONS IN THE DEVELOPMENT OF BLEEDING AND ISCHEMIA SCORES FOR EAST ASIANS. East Asian researchers have developed several thrombosis and bleeding risk scores based on the characteristics of the East Asian population, such as the Asian DAPT score, CREDO-Kyoto risk score, and BRIC-ACS score (**Supplemental Table 1**).²⁸⁻³⁰ There is currently a lack of a comprehensive scoring system or standardized tool that can be used to assess the risk of bleeding at different stages covering all comers. These ischemia-bleeding scores have shown some predictive values in the East Asian population, but require further validation in larger sample sizes. Meanwhile, large-scale studies should be conducted in more East Asian countries to revise and update the assessment tools and improve the accuracy of thrombotic and bleeding risk prediction considering changing environmental and clinical circumstances.

Previous studies have identified varying correlations between risk scores and actual clinical events across different races.^{31,32} Several genetic and epigenetic factors have been suggested to explain the lower

incidence of atherosclerotic cardiovascular disease (ASCVD) in the East Asian population. Biomarkers or surrogates reflecting atherothrombotic cardiovascular (CV) risks may provide valuable insights into racial differences in the incidence and prognosis of ASCVD. During guideline-directed medical therapy, East Asians exhibit lower biomarker levels of residual atherothrombotic CV risks compared with Caucasians (especially inflammation and coagulation activity), which may significantly contribute to the lower morbidity and mortality rates associated with ASCVD in East Asians compared with Western populations (**Table 3**).³¹ Therefore, risk scoring system based on clinical characteristics may not reflect the realistic risk of clinical events across the races.

RECOMMENDATIONS.

- Before initiation and during antiplatelet treatment in East Asian CAD patients, bleeding and ischemia risk stratification should be performed. The choice and duration of antiplatelet regimens largely depend on the balance between each individual's bleeding and ischemia risks.
- In the East Asian population, patients with high bleeding risk can be characterized by the following features: elderly age (≥ 75 years), low body weight (men < 55 kg, women < 50 kg), frailty, history of stroke, renal insufficiency, severe liver dysfunction, heart failure, peripheral artery disease, history of bleeding requiring treatment, recent major surgery or major trauma, active malignancy, thrombocytopenia (platelet count $< 100 \times 10^9/L$), anemia (hemoglobin < 110 g/L), long-term use of oral anti-coagulant/nonsteroidal anti-inflammatory drug/steroid, and undeferrable major surgery during DAPT period.
- In the East Asian population, patients with high ischemic risk can be characterized by the following features: diabetes, history of recurrent myocardial infarction, multivessel CAD, polyvascular disease, premature or accelerated CAD, concomitant systemic inflammatory disease, severe chronic kidney disease (CKD), atrial fibrillation, heart failure, anemia, history of complex revascularization, history of stent thrombosis on antiplatelet treatment, at least 3 stents implanted, at least 3 lesions treated, and total stent length > 60 mm.

INITIAL THERAPY, DURATION AND DE-ESCALATION OF DAPT IN ACS PATIENTS

INITIAL ANTIPLATELET THERAPY. Platelet activation-mediated thrombosis is the main pathophysiological mechanism of ACS, and platelet activation and aggregation play a key role in its development and

TABLE 1 Risk Factors for High Bleeding Risk in East Asian CAD Patients

Major Criteria	Minor Criteria
- Low body weight (men <55 kg, women <50 kg), frailty (elderly women, patients at risk of falls)^a - Severe CKD (hemodialysis): patients with eGFR <30 mL/min/1.73 m² - Moderate to severe anemia: hemoglobin <11 g/dL - HF, especially elderly HF patients undergoing PCI^a - Long-term oral anticoagulation - Peripheral artery disease^a - Active malignancies: active malignancies (diagnosed within 12 mo and/or continue to require treatment, including surgery, chemotherapy, or radiation) - History of nontraumatic bleeding events: gastrointestinal or urethral bleeding requiring hospitalization or blood transfusion within 6 months, or recurrent bleeding at any time - Moderate or severe baseline thrombocytopenia (platelet count <100 × 10⁹/L) - Chronic bleeding diathesis - Liver cirrhosis with portal hypertension - Previous spontaneous ICH (at any time) - Previous traumatic ICH within the past 12 mo - Presence of a brain arteriovenous malformation - Moderate or severe ischemic stroke within the past 6 mo - Major surgery without delay is planned during dual antiplatelet therapy - Recent major surgery or major trauma within 30 d before PCI	- Age ≥75 y, especially over 80 y - Moderate CKD: eGFR: 30 to <60 mL/min/1.73 m² - Mild anemia: hemoglobin 11 to <13.0 g/dL for men and 11 to <12.0 g/dL for women - Long-term use of oral nonsteroidal anti-inflammatory drugs or steroids - First nontraumatic bleeding event requiring hospitalization or transfusion within the past 6-12 mo - Any ischemic stroke at any time not meeting the major criterion

^aRisk factors suggested from the Japanese-HBR score.²⁴
CAD = coronary artery disease; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HBR = high bleeding risk; ICH = intracerebral hemorrhage; PCI = percutaneous coronary intervention.

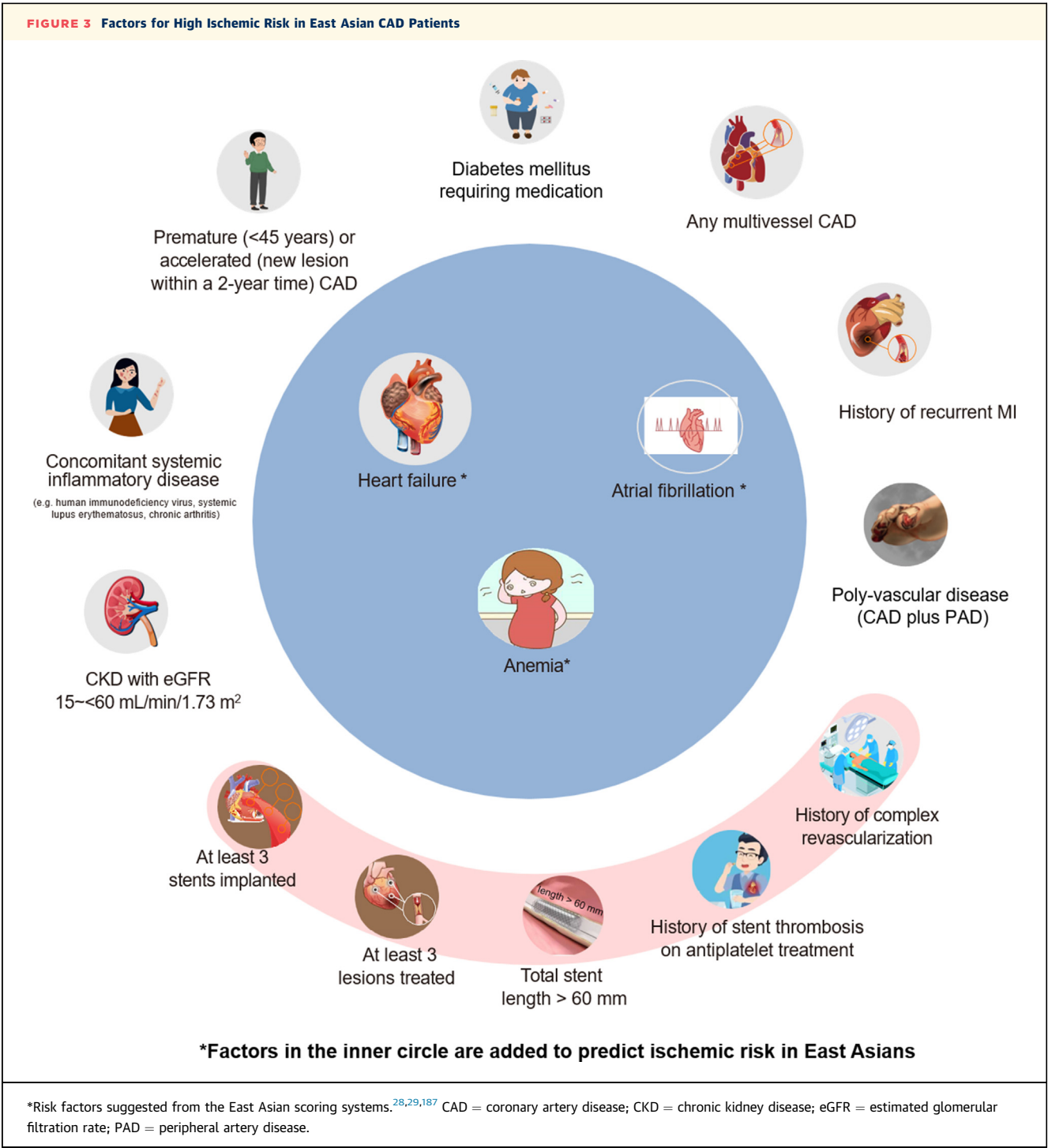
progression. Antiplatelet agents are therefore used throughout the treatment of ACS.^{33,34} Following PCI, the risk of ischemic events still remains high in the early stages. Therefore, initial treatment with DAPT is necessary to reduce the risk of thrombosis.^{10,24,35} At present, the commonly used DAPT regimen in ACS patients is mainly a combination therapy with a platelet cyclooxygenase-1 (COX-1) inhibitor and a P2Y₁₂ inhibitor.

ORAL ANTIPLATELET THERAPY. Platelet COX-1 inhibitors. Aspirin. A representative agent of COX-1 inhibitors is aspirin, which inhibits platelet aggregation and thrombosis by inhibiting the production of platelet COXs, blocking arachidonic acid oxidation, and thereby reducing thromboxane A₂ synthesis.³⁶ Aspirin has been a basic drug in antiplatelet therapy. The CURRENT-OASIS 7 (Clopidogrel and Aspirin Optimal Dose Usage to Reduce Recurrent Events—Seventh Organization to Assess Strategies in Ischemic Symptoms) study showed that there was no statistical difference between high-dose (300-325 mg/d) and low-dose aspirin (75-100 mg/d) in reducing the incidence of the primary endpoint (a composite of CV death, MI, and stroke)³⁷; however, the high-dose aspirin significantly increased the risk of gastrointestinal bleeding. Therefore, it is recommended by the ESC/EACTS guidelines that aspirin can be used for

antiplatelet therapy and that a low dose is superior to a high dose in ACS patients.³⁸

Indobufen. Indobufen reversibly inhibits COX-1, with a low inhibition rate on prostaglandins, mild gastrointestinal reactions, and low bleeding risks, which can be considered as an alternative therapy for patients with aspirin intolerance.³⁹ In the OPTION (Randomized Controlled Trial of Indobufen Versus Aspirin After Coronary Drug-Eluting Stent Implantation) study including 4,551 Chinese patients with drug-eluting stent (DES) implantation, compared with aspirin plus clopidogrel combination, indobufen plus clopidogrel combination significantly reduced the risk of the primary endpoint (1-year composite of CV death, nonfatal MI, ischemic stroke, definite or probable stent thrombosis, or Bleeding Academic Research Consortium [BARC] bleeding type 2, 3, or 5) (absolute difference: -1.63%; $P_{\text{noninferiority}} < 0.001$; HR: 0.73; $P = 0.015$), while the incidence of bleeding with indobufen plus clopidogrel combination was significantly lower than that in the aspirin plus clopidogrel combination (HR: 0.63; $P = 0.002$).⁴⁰

P2Y₁₂ receptor inhibitors. Adenosine diphosphate (ADP) is a critical agonist in the process of platelet activation and aggregation. The P2Y₁₂ inhibitors can prevent ADP from binding to platelet surface receptors, effectively weaken the cascade reaction of ADP, and



reduce the cascade of platelet aggregation.⁴¹ At present, the commonly used P2Y₁₂ inhibitors are clopidogrel, ticagrelor, and prasugrel.

Clopidogrel. Clopidogrel is a second-generation thienopyridine P2Y₁₂ inhibitor that reduces platelet aggregation by irreversibly and selectively inhibiting the P2Y₁₂ receptors on the platelet surface. The

CURE (Clopidogrel in Unstable angina to prevent Recurrent ischemic Events) study (12,562 patients presented with ACS) showed that DAPT regimen with clopidogrel plus aspirin significantly reduced the incidence of ischemic events (relative risk [RR]: 0.80; 95% CI: 0.72-0.90; *P* < 0.001) compared with aspirin plus placebo, laying the foundation for

TABLE 2 Risk Factors for High Ischemic Risk in East Asian CAD Patient

General Clinical Characteristics	Technical Aspects
- DM requiring medication - History of recurrent MI - Any multivessel CAD - Polyvascular disease (CAD plus PAD) - Premature (<45 y) or accelerated (new lesion within a 2-y time frame) CAD - Concomitant systemic inflammatory disease (eg, HIV, systemic lupus erythematosus, chronic arthritis) - CKD with eGFR 15–<60 mL/min/1.73 m² - Atrial fibrillation^a - Heart failure^a - Anemia^a	- At least 3 stents implanted - At least 3 lesions treated - Total stent length >60 mm - History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, CTO, stenting of last patent vessel) - History of stent thrombosis on antiplatelet treatment
^a Risk factors suggested from the East Asian scoring systems. ^{28,29,187} CAD = coronary artery disease; CKD = chronic kidney disease; CTO = chronic total occlusion; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; MI = myocardial infarction.	

clopidogrel usage in DAPT.⁴² The COMMIT (CLOpidogrel and Metoprolol in Myocardial Infarction Trial) (45,852 Chinese patients presenting with AMI), PCI-CLARITY (PCI-Clopidogrel as Adjunctive Reperfusion Therapy) (1,863 ST-segment elevation myocardial infarction [STEMI] patients), and CREDO (Clopidogrel for the Reduction of Events During Observation) (2,116 PCI-treated patients) trials also confirmed that clopidogrel plus aspirin, compared with aspirin alone, significantly reduced the rates of adverse clinical outcomes including all-cause mortality, CV death, and major vascular

events.⁴³⁻⁴⁵ The CAPRIE (Clopidogrel Versus Aspirin in Patients at Risk of Ischaemic Events) study (19,185 patients with recent ischemic stroke, recent MI, or symptomatic PAD) showed that clopidogrel monotherapy compared with aspirin monotherapy was more effective (relative-risk reduction, 8.7%; 95% CI: 0.3-16.5; $P = 0.043$) in reducing the combined risk of ischemic stroke, MI, or vascular death.⁴⁶

The COSTIC (Comparison Of Efficacy and Safety Between Ticagrelor and Clopidogrel In Chinese) and BRIC-ACS (Bleeding Risk in Real World Chinese Acute

TABLE 3 Racial Differences in Atherothrombotic Cardiovascular Risks³¹

Factors	Racial Difference	Component
Lipid profile		
High LDL cholesterol	Hispanics = Caucasians > East Asians > Blacks	Atherosclerosis
Low HDL cholesterol	Hispanics > Caucasians ≥ East Asians > Blacks	Atherosclerosis
High triglyceride	East Asians > Hispanics > Caucasians > Blacks	Atherosclerosis
Lipoprotein(a) level	Blacks > Caucasians > Hispanics > East Asians	Atherosclerosis
Inflammation		
CRP level	Blacks > Hispanics > Caucasians > East Asians	Inflammation
Platelet		
Platelet count	Blacks > Hispanics > Caucasians	Hemostasis
Regulation of Gq pathway after PAR-4 stimulation	Blacks > Caucasians	Platelet activation
Response to clopidogrel	Caucasians = Hispanics > Blacks > East Asians	Antiplatelet effect
Response to ticagrelor	East Asians > Caucasians = Hispanics > Blacks	Antiplatelet effect
Coagulation		
Factor V Leiden allelic variant	Caucasians (~5%) > Blacks (~1.5%) > Hispanics = Asians	Coagulant activity
Prothrombin G20210A allelic variant	Caucasians (2%-5%) > Blacks = Hispanics = Asians	Coagulant activity
von Willebrand factor level	Blacks > Caucasians = Hispanics ≥ East Asians	Endothelial adhesion factor
Fibrinogen, factor VII and VIII, and thrombin levels	Blacks ≥ Caucasians = Hispanics ≥ East Asians	Coagulant activity
D-dimer level	Blacks > Caucasians = Hispanics > East Asians	Prothrombotic and hypofibrinolytic state
Anticlotting activity		
Effect of activated protein C	Asians = Hispanics ≥ Blacks > Caucasians	Anticoagulant activity
PAI-1 level	Caucasians > Hispanics > East Asians ≥ Blacks	Antifibrinolytic activity
CRP= C-reactive protein; HDL = high-density lipoprotein; LDL = low-density lipoprotein; PAI-1 = plasminogen activator inhibitor-1; PAR = proteinase-activated receptor.		

Coronary Syndrome Patients) trials conducted in a Chinese population showed that the clopidogrel plus aspirin regimen had a significantly lower risk of bleeding after discharge, and a similar risk of major adverse cardiovascular events (MACE) compared with the ticagrelor and aspirin regimen.^{30,47} In a cohort analysis including 32,441 Taiwanese patients presenting with AMI, DAPT including ticagrelor vs clopidogrel had similar incidences of the primary efficacy endpoint, but DAPT with clopidogrel showed a significantly lower risk of BARC type 2 bleeding than DAPT with ticagrelor.⁴⁸

Ticagrelor. Ticagrelor is a cyclopentyl triazole pyrimidine drug and a novel oral P2Y₁₂ inhibitor with a direct effect and reversible binding activity. It has been demonstrated that the exposure of major active metabolites of ticagrelor is higher in the East Asian population compared with the Western population.^{49,50} The pivotal international PLATO (Platelet Inhibition and Patient Outcomes) study showed that, compared with clopidogrel, ticagrelor reduced the rate of MACE with no significant differences in the rates of PLATO-defined bleeding events.⁵¹ However, the PHILO (Ticagrelor vs. Clopidogrel in Japanese, Korean and Taiwanese Patients With Acute Coronary Syndrome) study performed in East Asian patients showed different results compared to the PLATO study, which found that the risk of major bleeding in patients treated with ticagrelor was about 2.2 times that in the multinational population and there was no reduction in the MACE rate compared with the clopidogrel group.⁵² The TICA-KOREA (Ticagrelor Versus Clopidogrel in Asian/Korean Patients with ACS Intended for Invasive Management) study showed that the incidence of clinically significant bleeding was significantly lower in the clopidogrel group than in the ticagrelor group (5.3% vs 11.7%; $P = 0.002$), and the risk of PLATO major bleeding in the clopidogrel group was also lower compared with the ticagrelor group (4.1% vs 7.5%; $P = 0.04$).⁵³

Prasugrel. As an oral prodrug, prasugrel can only exert its antiplatelet effects through its active metabolites generated by the oxidative reaction of liver enzymes. The TRITON-TIMI (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction) 38 study demonstrated that in ACS patients scheduled for PCI, treatment with prasugrel, compared with clopidogrel, reduced the rate of adverse CV events within 15 months, whereas the incidence of major bleeding events increased with prasugrel (2.4% vs 1.8%; HR: 1.32; 95% CI: 1.03-1.68; $P = 0.03$).⁵⁴ In a cohort study including ACS patients from South

Korea, 56,216 patients (79.5%) received clopidogrel, 11,402 patients (16.1%) received ticagrelor, and 3,097 patients (4.4%) received prasugrel. No significant differences in efficacy were observed among the groups. However, treatment with prasugrel was associated with a higher risk of any bleeding (HR: 1.23; $P = 0.01$) and major bleeding (HR: 1.50; $P = 0.04$) compared with clopidogrel.⁵⁵ A retrospective cohort study⁵⁶ evaluated 2,770 Japanese patients with ACS who underwent PCI and received either low-dose prasugrel (3.75 mg daily) or clopidogrel in combination with aspirin. Results suggested that bleeding events were higher among patients receiving low-dose prasugrel than among patients receiving clopidogrel, with no difference in ischemic events between the 2 groups. In addition, half-dose (5 mg daily) vs standard-dose prasugrel (10 mg daily) showed a lower risk of serious bleeding (HR: 0.48; 95% CI: 0.32-0.73; $P = 0.0007$) and a similar rate of ischemic events (HR: 0.76; 95% CI: 0.40-1.45; $P = 0.40$) in Korean ACS patients.⁵⁷

Taken together, the risk of serious bleeding in East Asian ACS patients has been higher with ticagrelor or prasugrel than with clopidogrel, whereas no significant differences are observed in the incidence of ischemic events. These findings should be considered to guide the selection of DAPT strategies in East Asian patients with ACS.⁵⁸⁻⁶²

Selective phosphodiesterase-3 inhibitor. Cilostazol.

Cilostazol works by selectively inhibiting the activity of phosphodiesterase-3, which obstructs the degradation and transformation of cyclic adenosine monophosphate (cAMP). This leads to an increase in the cAMP levels in various cells including platelets, vascular smooth muscle cells, and endothelial cells. As a result, cilostazol exerts antiplatelet aggregation, promotes vascular dilation, and reduces the risk of vascular obstruction.⁶³ In a Korean retrospective study, 4,203 STEMI patients who underwent primary PCI with DES were analyzed, triple antiplatelet group (aspirin plus clopidogrel plus cilostazol) had a similar incidence of major bleeding events but a significantly lower incidence of in-hospital mortality compared with the dual group (aspirin plus clopidogrel), clinical outcomes at 8 months showed that the triple group had a significantly lower incidence of MACE (OR: 0.74; $P = 0.019$) than the dual group.⁶⁴

RECOMMENDATIONS.

- For East Asian patients with ACS, the initial DAPT regimen should be selected based on the individual ischemic and bleeding risks. Patients with high ischemic risk should begin with aspirin plus a

potent P2Y₁₂ inhibitor, while those with high bleeding risk should preferably start with aspirin plus clopidogrel.

- For patients with aspirin intolerance or high bleeding risk, DAPT with indobufen can be chosen as an alternative to DAPT with aspirin.

DURATION OF DAPT. Twelve-month maintenance has been a standard duration of the DAPT strategy for patients with ACS.^{4,5,8,65} The DAPT and PEGASUS-TIMI 54 (Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54) studies have found that the benefits of ischemia reduction from an extended DAPT maintenance (>12 months) were partially offset by an increased risk of bleeding in stabilized CAD patients with high ischemic risk (eg, a history of MI in the past 1 to 3 years with ≥ 1 ischemic risk factor).^{66,67} A study based on risk stratification showed that for patients with a DAPT score ≥ 2 , the extended duration of DAPT was associated with reduced ischemic events and smaller increases in bleeding compared with those with low scores.⁶⁸

A wave of research on shortening the duration of DAPT has gained momentum, especially from East Asian countries. In the MASTER-DAPT (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation with an Abbreviated versus Standard DAPT Regimen) trial (4,579 CAD patients at HBR), patients were implanted with bioresorbable polymer-coated stent and randomized after 1-month DAPT to abbreviated or nonabbreviated antiplatelet strategy; 1-month DAPT was noninferior to the continuation of therapy for at least 2 (5 if without oral anticoagulation) additional months for the occurrence of ischemic events (7.5% vs 7.7%; difference, -0.23% ; 95% CI: -1.80 to 1.33 ; $P < 0.001$ for noninferiority) with a lower incidence of major or clinically relevant bleeding event (6.5% vs 9.4%; difference, -2.82% ; 95% CI: -4.40 to -1.24 ; $P < 0.001$ for superiority).⁶⁹ Furthermore, a subgroup analysis of this trial showed that the results were consistent across geographical regions (Europe, East Asia, and others).⁷⁰ However, this study had several limitations to be considered when drafting this consensus: first, only 48.3% of the whole set were ACS patients; second, the limited number of patients ($n = 274$; 5.98%) were enrolled from 4 East Asian countries (Japan, South Korean, Singapore, and Vietnam). The SMART-CHOICE study included 2,993 Korean patients undergoing DES implantation. After 3-month default DAPT maintenance, patients were randomized to the

P2Y₁₂ inhibitor monotherapy group or to the DAPT group in a 1:1 ratio. Clopidogrel was used as the P2Y₁₂ inhibitor in 1,149 patients (76.9%) in the monotherapy group and 1,163 (77.6%) in the DAPT group. P2Y₁₂ inhibitor monotherapy compared with DAPT showed similar efficacy in preventing the recurrence of ischemic events, with a lower risk of bleeding in these patients.¹⁹ The STOPDAPT-2 (Short and Optimal Duration of Dual Antiplatelet Therapy After Everolimus-Eluting Cobalt-Chromium Stent-2) trial included 3,045 Japanese patients (38% with ACS) who underwent PCI. Patients were randomized either to 1-month DAPT (aspirin plus clopidogrel or prasugrel) followed by clopidogrel monotherapy or to 12-month DAPT with aspirin and clopidogrel. Clopidogrel monotherapy after 1-month DAPT, compared with 12-month DAPT, resulted in a significantly lower rate of bleeding events (0.41% vs 1.54%; HR: 0.26; 95% CI: 0.11-0.64; $P = 0.004$) without difference in the risk of ischemic events (1.96% vs 2.51%; HR: 0.79; 95% CI: 0.49-1.29; $P = 0.34$).⁷¹ Another STOPDAPT-2 ACS study revealed that noninferiority in net clinical benefit was not achieved with a 1- to 2-month DAPT regimen compared with the standard 12-month DAPT regimen after DES implantation in 4,136 Japanese ACS patients (3.2% vs 2.8%; HR: 1.14; 95% CI: 0.80-1.62; P for noninferiority = 0.06).⁷² Although there was a decrease in major bleeding events (absolute difference, -0.63% ; HR: 0.46; 95% CI: 0.23-0.94), CV events still showed an increasing trend (absolute difference, 0.90%; HR: 1.50; 95% CI: 0.99-2.26). In the HOST-IDEA (Harmonizing Optimal Strategy for Treatment of Coronary Artery Stenosis—Coronary Intervention With Next Generation Drug-Eluting Stent Platforms and Abbreviated Dual Antiplatelet Therapy) trial, including 2,013 Korean patients (55.1% were ACS) undergoing DES implantation, 3- to 6-month DAPT was noninferior to 12-month DAPT in terms of target lesion failure (HR: 0.98; 95% CI: 0.56-1.71; $P = 0.94$) and major bleeding (HR: 0.82; 95% CI: 0.41-1.61; $P = 0.56$).⁷³

Based on the previously mentioned evidence and real-world clinical practice in East Asia, it is reasonable for ACS patients with high bleeding risk to receive abbreviated DAPT duration, followed by long-term treatment with antiplatelet monotherapy, preferably with a P2Y₁₂ inhibitor.

RECOMMENDATIONS. Refer to [Figure 4](#) for guidance.

- In East Asian ACS patients with high bleeding risk (meeting the HBR criteria for East Asian populations), an abbreviated DAPT with aspirin plus clopidogrel is preferred, followed by long-term treatment with antiplatelet monotherapy,

Treatment preferences within each box are shown from above to below, whereas treatments within the same line are sorted in alphabetical order. ACS = acute coronary syndrome; CCS = chronic coronary syndromes; FDC = fixed-dose combination of 100-mg aspirin plus 75-mg clopidogrel; PCI = percutaneous coronary intervention.

The SWAP-4 (Switching Antiplatelet Therapy-4) study indicated that switching from ticagrelor to clopidogrel may lead to platelet hyperreactivity, but

the use of a loading dose of clopidogrel prior to the switch can reduce this effect.⁷⁵ Given the half-life of ticagrelor and the time required for new platelets to be released into the blood, it is recommended to give a 300-mg loading dose of clopidogrel within 24 hours after the last dose of ticagrelor, followed by DAPT maintenance with clopidogrel 75 mg a day for 12 months.⁷⁶ The TOPIC (Timing of Platelet Inhibition After Acute Coronary Syndrome) study was the earliest de-escalation investigation in 2017, in which 646 ACS patients who underwent PCI were included to receive ticagrelor or prasugrel plus aspirin for 1 month and then randomized to either maintaining this DAPT regimen or switching to clopidogrel plus aspirin (without clopidogrel loading dose).⁷⁷ Compared with the maintenance regimen, switching to clopidogrel showed no significant difference in reducing ischemic events but significantly reduced the bleeding events (HR: 0.30; 95% CI: 0.18-0.50; $P < 0.01$). The TALOS-AMI (Ticagrelor versus Clopidogrel in Stabilized Patients with Acute Myocardial Infarction) study including AMI patients from South Korea ($n = 2,697$) explored the efficacy of the DAPT strategy with ticagrelor switched to clopidogrel at 1 month after PCI.⁷⁸ Compared with the continuing use of ticagrelor, the de-escalation strategy with clopidogrel was equally effective in preventing ischemic events and significantly reduced the incidence of major bleeding (3.0% vs 5.6%, HR: 0.52; $P = 0.0012$).⁷⁸ These results demonstrated that switching from a potent P2Y₁₂ inhibitor to clopidogrel during the stabilized period reduced bleeding risk without increasing ischemic risk in East Asian patients who are not at high ischemic risk.

De-escalation DAPT strategy guided by platelet function test (PFT) or genotyping can be applicable in clinical practice. The TROPICAL-ACS (Testing Responsiveness To Platelet Inhibition On Chronic Antiplatelet Treatment For Acute Coronary Syndromes) study performed in European countries suggested that switching from prasugrel to clopidogrel as guided by the PFTs was not inferior to standard prasugrel treatment in terms of the net clinical benefit at 1 year.⁷⁹ The TAILOR-PCI study conducted in North America and Korea explored *CYP2C19* genotype-guided antiplatelet de-escalation strategy and found that compared with conventional clopidogrel therapy after PCI procedure, genotype-guided individualized treatment with P2Y₁₂ inhibitor did not significantly reduce the ischemic events (HR: 0.84; 95% CI: 0.65-1.07; $P = 0.16$) at 1 year in CAD patients after PCI.⁸⁰ The POPular Genetics study also showed that the genotype-guided de-escalation therapy did not reduce the incidence of ischemic

events, but significantly reduced the incidence of major bleeding.⁸¹ These results demonstrated that a guided de-escalation strategy may be better but still needs more evidence. Current evidence does not support the routine usage of PFT and genotyping to guide antiplatelet regimens.^{82,83}

Dose reduction of potent P2Y₁₂ inhibitor. Reducing the dose of prasugrel or ticagrelor in DAPT combinations is a P2Y₁₂-specific de-escalation strategy that may be desired when concerns exist regarding high exposure to the active metabolite of potent P2Y₁₂ inhibitors in the East Asian population. However, there are only limited data on this de-escalation strategy during the first year after ACS. In the HOST-REDUCE-POLYTECH-ACS (Harmonizing Optimal Strategy for Treatment of Coronary Artery Diseases—Comparison of Reduction of Prasugrel Dose or Polymer Technology in ACS Patients) study, a halved dose of prasugrel at 1 month reduced 1-year NACE, which is mainly contributed by reducing major bleeding events (HR: 0.48; 95% CI: 0.32-0.73; $P = 0.0007$), compared with the conventional group.⁵⁷ The PEGASUS-TIMI 54 trial demonstrated that a dosing regimen of ticagrelor 60 mg twice daily can be used in stabilized AMI patients.⁶⁷ More evidence is needed for the dose reduction strategy, especially for East Asian patients.

Discontinuation. A lot of large-scale RCTs and guidelines published in recent years suggested that discontinuation of aspirin vs P2Y₁₂ inhibitor would be a better choice following DAPT maintenance in ACS patients. The 2020 ESC guideline for ACS recommends that aspirin can be discontinued at 3 to 6 months, with continuation of the P2Y₁₂ inhibitor (Class IIa).⁴ The 2021 ACC/AHA/SCAI guideline for coronary revascularization recommends that aspirin can be discontinued at 1 to 3 months, and the P2Y₁₂ inhibitor continued (Class IIa).⁸⁴ The 2023 ESC guideline for ACS recommends that single antiplatelet therapy (preferred P2Y₁₂ inhibitor) after 3 to 6 months of DAPT for patients who are event-free and not at high ischemic risk should be considered (Class IIa).⁸ For patients with HBR, aspirin or P2Y₁₂ inhibitor monotherapy is recommended after 1 month of DAPT (Class IIb).

A lot of evidence supported the de-escalation strategy of discontinuation, especially for East Asian patients. In the TWILIGHT (Ticagrelor with Aspirin or Alone in High-Risk Patients after Coronary Intervention) study which enrolled 9006 PCI-treated patients (nearly 40% were Chinese patients), 3 months of DAPT followed by ticagrelor monotherapy showed reduced bleeding risk and similar risk in ischemic events compared with 12 months of DAPT.⁸⁵ In the

TICO study (3,056 Korean patients with ACS after PCI), discontinuation at 3 months with transition to ticagrelor monotherapy was superior for 1-year NACE (3.9% vs 5.9%; HR: 0.66; 95% CI: 0.48-0.92; $P = 0.01$) compared with the conventional treatment.¹⁸ In the SHARE (Short-Term Dual Antiplatelet Therapy After Deployment of Bioabsorbable Polymer Everolimus-Eluting Stent) study (1,387 Korean patients after PCI), P2Y₁₂ inhibitor monotherapy (62.5% on clopidogrel) after 3 months of DAPT was noninferior to 12 months of DAPT in terms of NACE between 3 and 12 months of follow-up (1.7% vs 2.6%; 1-sided 95% CI: -2.64 to 0.77 percentage; $P < 0.001$ for noninferiority).⁸⁶ The STOPDAPT-2 ACS study (4,136 Japanese patients with ACS underwent PCI) demonstrated that discontinuation at 1 to 2 months with transition to clopidogrel monotherapy was not noninferior for 1-year NACE.⁷² In the ULTIMATE-DAPT (Ticagrelor alone versus ticagrelor plus aspirin from month 1 to month 12 after percutaneous coronary intervention in patients with acute coronary syndromes) study, which included 3,400 patients (88.1% from Chinese) with ACS who underwent PCI, 1 month of DAPT followed by ticagrelor monotherapy showed reduced bleeding risk (2.1% vs 4.6%; HR: 0.45; 95% CI: 0.30-0.66; $P < 0.0001$) and a similar rate in ischemic events (3.6% vs 3.7%; HR: 0.98; 95% CI: 0.69-1.39; $P = 0.89$ for superiority) compared with continued DAPT following PCI in ACS patients, which may give high-quality evidence (placebo-based trial) for discontinuation of aspirin in East Asian patients.⁸⁷ In the T-PASS (Ticagrelor Monotherapy in Patients Treated With New-Generation Drug-Eluting Stents for Acute Coronary Syndrome) study (2,850 Korean ACS patients underwent PCI), ticagrelor monotherapy after <1 month of DAPT (mean, 16 days) reduced NACE (2.8% vs 5.2%; HR: 0.54; 95% CI: 0.37-0.80; $P = 0.002$ for superiority) compared with 12 months of DAPT in ACS patients.⁸⁸ Because ischemic risk in ACS patients can be higher in the first month following PCI, de-escalation within 1 month should be very cautious, which is not recommended in guidelines. A meta-analysis including 23 randomized trials demonstrated the different balance between ischemic and bleeding events between DAPT de-escalation and conventional DAPT. In Caucasians, reduced DAPT intensity increased MACE (OR: 1.20; 95% CI: 1.09-1.31; $P < 0.0001$) without impacting bleeding, whereas in East Asians, this strategy reduced major bleeding (OR: 0.71; 95% CI: 0.53-0.95; $P = 0.02$) without affecting MACE. Abbreviation of DAPT duration did not impact MACE or major bleeding in Caucasians, whereas this strategy reduced major bleeding (OR: 0.60; 95% CI: 0.40-0.91; $P = 0.02$) without impacting MACE in East Asians.

Taken together, de-escalation of DAPT intensity, or shortening DAPT duration can be considered a default strategy in East Asians presented with ACS who are on a standard dose of potent P2Y₁₂ inhibitor, particularly after the acute phase (~1 month post-PCI).⁸⁹

RECOMMENDATIONS.

- For ACS patients initially receiving aspirin with ticagrelor or prasugrel, active de-escalation to aspirin with clopidogrel after 1 month can be considered. If an adverse reaction such as dyspnea or bleeding is observed during the initial treatment, or initiation of anticoagulant therapy is necessary, early de-escalation by DAPT with aspirin plus clopidogrel can be considered.
- Routine use of platelet function- or genotype-guided de-escalation for antiplatelet therapy is not recommended.
- Due to the limited clinical evidence for dose reduction of potent P2Y₁₂ inhibitor, this de-escalation strategy for ACS patients is recommended for patients receiving DAPT with a standard dose of prasugrel.
- For ACS patients initially receiving DAPT with aspirin plus ticagrelor or prasugrel, who remain event-free after 1 month and are not at high ischemic risk, an abbreviated DAPT duration, followed by antiplatelet monotherapy (preferably with P2Y₁₂ inhibitor) can be considered.

ANTIPLATELET THERAPY MANAGEMENT OF CCS

CAD is a dynamic process involving atherosclerotic plaque accumulation and change in coronary circulation function, with a relatively stable stage, and can also be unstable because of plaque rupture, plaque erosion, and calcified nodules.^{90,91} Previously, stable CAD was generally considered to consist of 3 types, namely, chronic stable exertional angina, ischemic cardiomyopathy, and a stable course of disease after ACS. In the 2019 ESC Guidelines for Diagnosis and Management of Chronic Coronary Syndromes,⁹² stable CAD is renamed as “CCS,” which includes 6 common clinical conditions. The new classification proposed in the CCS guideline better reflects the dynamic pathological characteristics of CAD, indicating that the stability in the nonacute stage is relative and the risk of development to ACS remains at any time. Therefore, clinicians should pay more attention to the long-term management of CAD.

DUAL ANTIPLATELET THERAPY IN PATIENTS WITH CCS. Currently, the clinical studies specifically investigating the duration of DAPT in patients with CCS are limited. The PEGASUS-TIMI 54 study found

that for stabilized CAD patients with a history of MI and ≥ 1 risk factor for atherosclerotic thrombosis, DAPT with reduced-dose ticagrelor (60 mg twice a day) reduced MACE within 3 years (7.77% vs 9.04%; HR: 0.84; 95% CI: 0.74-0.95; $P = 0.004$).⁶⁷ Compared with aspirin monotherapy, there was no significant difference in the incidence of intracranial hemorrhage (ICH) or fatal bleeding (0.71% vs 0.60%). The study results were not affected by the baseline history of the PCI procedure.⁶⁷ Therefore, long-term DAPT maintenance may be considered for East Asian patients with high ischemic risk (eg, a history of MI with risk factors for atherosclerotic thrombosis). 3 studies in the Korean population compared different DAPT durations after DES implantation. The DES LATE (Optimal Duration of Clopidogrel Therapy With DES to Reduce Late Coronary Arterial Thrombotic Event) study included 5,045 patients who were on 12-month DAPT without complications, results showed that an additional 24 months of DAPT vs aspirin alone did not reduce the risk of the composite end point of death from cardiac causes, MI, or stroke.⁹³ In the EXCELLENT (Efficacy of Xience/Pro-mus Versus Cypher to Reduce Late Loss After Stenting) study, 1,443 patients who underwent DES implantation were randomized to receive 6- or 12-month DAPT. The 6-month DAPT resulted in non-inferiority effects on the risk of target vessel failure at 12 months after implantation of DES compared with 12-month DAPT.⁹⁴ A total of 2,117 CAD cases in the RESET (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation) trial were randomized to receive 3-month DAPT following Endeavor zotarolimus-eluting stent implantation or 12-month DAPT following the other DES implantation.⁹⁵ The Endeavor zotarolimus-eluting stent +3-month DAPT was noninferior to the standard therapy in the occurrence of the composite endpoint (CV death, MI, stent thrombosis, target vessel revascularization, or bleeding) at 1 year. These results suggested that shortening the duration of DAPT should be considered in CCS patients with high bleeding risk.

The ALPHEUS (Assessment of Loading with the P2Y₁₂ inhibitor ticagrelor or clopidogrel to Halt ischemic Events in patients Undergoing elective coronary Stenting) study showed that ticagrelor-based DAPT was not superior to clopidogrel-based DAPT (OR: 0.97; 95% CI: 0.80-1.17; $P = 0.75$) in reducing periprocedural myocardial necrosis after elective PCI, but did increase the rate of minor bleeding (OR: 1.54; 95% CI: 1.12-2.11; $P = 0.007$), suggested that clopidogrel can be used for the standard treatment for patients undergoing elective PCI.⁹⁶ The COMPASS

(Cardiovascular Outcomes for People Using Anti-coagulation Strategies) study, including 27,395 patients with stable atherosclerotic vascular disease, found that the risks of primary endpoints (CV death, MI, or stroke) in the group with rivaroxaban and aspirin treatment were significantly lower than those in the aspirin monotherapy group (4.1% vs 5.4%; HR: 0.76; 95% CI: 0.66-0.86; $P < 0.001$) during a mean follow-up of 23 months, whereas the risk of major bleeding event was increased (3.1% vs 1.9%; HR: 1.70; 95% CI: 1.40-2.05; $P < 0.001$).⁹⁷ Relevant studies on DAPT duration in CCS patients undergoing PCI were summarized in [Supplemental Table 2](#).

LONG-TERM ANTIPLATELET MONOTHERAPY AFTER PCI. Long-term antiplatelet monotherapy is needed for patients with CAD after DAPT. In previous clinical practice, aspirin has been a common option for this monotherapy, but there are still many patients with aspirin intolerance caused by various factors such as the risk of bleeding, gastrointestinal injury, as well as triggering or worsening of respiratory symptoms. The exact prevalence of aspirin intolerance is unknown, but the prevalence of aspirin-induced asthma was about 3% in adults.^{98,99}

With the advent of P2Y₁₂ inhibitors that inhibit ADP from binding platelet surface receptors and thereby reducing platelet aggregation, these agents have been shown to be more effective in preventing ischemia than aspirin. The CAPRIE study including 19,185 patients with ischemic stroke, MI, or PAD showed that clopidogrel was more effective than aspirin in reducing CV adverse events (relative-risk reduction, 8.7%; 95% CI: 0.3%-16.5%; $P = 0.043$).¹⁰⁰ The HOST-EXAM (Harmonizing Optimal Strategy for Treatment of coronary artery stenosis-Extended Antiplatelet Monotherapy) study included 5,438 Korean patients who maintained DAPT without clinical events for 6-18 months after PCI with DES.¹⁰¹ Following DAPT, clopidogrel monotherapy significantly reduced the risk of the primary endpoint (all-cause death, MI, stroke, readmission caused by ACS, and major bleeding) over the 24-month follow-up compared with aspirin monotherapy (5.7% vs 7.7%; HR: 0.73; 95% CI: 0.59-0.90; $P = 0.0035$). The incidence of thrombotic composite endpoint was significantly lower in the clopidogrel group than in the aspirin group (3.7% vs 5.5%; HR: 0.68; $P = 0.0028$). In the extended follow-up of 5.8 years, the primary endpoint continued to exhibit a similar trend. Clopidogrel monotherapy may be an optimal antiplatelet strategy over aspirin monotherapy in DES-treated East Asian patients with high ischemic or bleeding risk.¹⁰² The latest OPT-BIRISK (Optimal Antiplatelet Therapy for High Bleeding and Ischemic

Risk Patients) study included 7,758 Chinese patients presented with ACS who are at both high bleeding and ischemic risk. After 9 to 12 months of DAPT following PCI, an extended 9-month clopidogrel monotherapy strategy significantly reduced clinically relevant bleeding events (BARC type 2, 3, or 5 bleeding) (2.5% vs 3.3%; HR: 0.75; 95% CI: 0.57-0.97; $P = 0.03$) compared with DAPT with clopidogrel.¹⁰³ In addition, the relative risk of MACE was significantly reduced by clopidogrel monotherapy (2.6% vs 3.6%; HR: 0.74, 95% CI: 0.57-0.96; $P = 0.02$ for superiority), which further confirmed the clopidogrel monotherapy regimen was superior to continued DAPT in reducing clinically relevant bleeding and MACE in East Asian patients. The PANTHER meta-analysis (P2Y₁₂ Inhibitor or Aspirin Monotherapy as Secondary Prevention in Patients With Coronary Artery Disease: An Individual Patient Data Meta-Analysis of Randomized Trials) (7 trials, 24,325 CAD patients) demonstrated that P2Y₁₂ inhibitor monotherapy may be preferred over aspirin monotherapy for long-term secondary prevention, showing a reduced ischemic risk (HR: 0.88; 95% CI: 0.79-0.97; $P = 0.012$) and a similar bleeding risk (HR: 0.87; 95% CI: 0.70-1.09; $P = 0.23$) over 2 years.¹⁰⁴ Other studies on long-term antiplatelet monotherapy in patients with CAD were summarized in [Supplemental Table 3](#).

RECOMMENDATIONS. Refer to [Figure 4](#) for guidance.

- For CCS patients who can tolerate DAPT without bleeding complications, long-term DAPT with clopidogrel is recommended for those with high ischemic risk and low bleeding risk.
- For CCS patients with high bleeding risk undergoing PCI, antiplatelet monotherapy with clopidogrel after 1 to 3 months of DAPT can be considered.
- Adding vascular-dose anticoagulant (eg, rivaroxaban 2.5 mg twice a day) to aspirin can be considered in CCS patients with high ischemic risk (meeting the COMPASS criteria⁹⁷) for long-term secondary prevention.
- Long-term maintenance of antiplatelet monotherapy with clopidogrel or aspirin is recommended for CCS patients. Clopidogrel monotherapy is preferred as an alternative to aspirin monotherapy for patients with high ischemic risk.

SPECIAL POPULATIONS

Given the risk of bleeding during antithrombotic treatment is relatively higher in the East Asian population compared to the Caucasian population,

features of HBR that are commonly associated with CAD—such as advanced age, combined use of oral anticoagulant, stroke, gastrointestinal bleeding, or CKD—pose additional challenges to cardiologists. The use of antiplatelet therapy in these special populations should be approached with increased caution.

ELDERLY POPULATION. The elderly population, typically defined as individuals aged 75 years and older, is rapidly increasing in East Asian countries. This group is well known to have an elevated risk of major bleeding, likely caused by factors such as frailty, low body weight, and multiple comorbidities (eg, anemia, chronic kidney disease, heart failure, and malignancy). Managing medication for this population is particularly challenging caused by the need for multiple medications addressing their comorbidities and issues with poor medication compliance.¹⁰⁵

The POPular AGE study ($n = 1,002$) was the first comparative study focusing on the net clinical benefits of antiplatelet agents in ACS patients over the age of 70 years.¹⁰⁶ DAPT with clopidogrel significantly reduced the bleeding incidence compared with DAPT with ticagrelor or prasugrel (18% vs 24%; HR: 0.71; 95% CI: 0.54-0.94; $P = 0.02$ for superiority), and the efficacy was comparable, while DAPT with clopidogrel showed better compliance (premature discontinuation: 22% vs 47%). The SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry (14,005 ACS patients aged ≥ 80 years) showed that DAPT with ticagrelor increased the risk of death by 17% and the risk of bleeding by 48% compared with DAPT with clopidogrel.¹⁰⁷ A cohort study including 18,244 Chinese ACS patients aged ≥ 75 years found that the risk of in-hospital major bleeding in patients receiving ticagrelor treatment was significantly increased than in those receiving clopidogrel (HR: 1.45; 95% CI: 1.09-1.91) with comparable risks of in-hospital MACE (HR: 1.12; 95% CI: 0.92-1.35).¹⁰⁸ Another observational study from China (2,775 ACS patients aged ≥ 75 years) showed that ticagrelor treatment did not significantly reduce the risk of the primary efficacy outcome ($P = 0.156$) while significantly increasing the rates of all-cause death (HR: 1.69; $P = 0.040$) and major bleeding (HR: 2.20; $P = 0.035$) compared with clopidogrel.⁶²

The long-term risk of disabling or fatal bleeding events caused by antiplatelet therapy is higher in patients ≥ 75 years of age compared with younger patients.¹⁰⁹ Low-dose aspirin monotherapy, despite its benefit in secondary prevention of CV disease, still

comes with a high risk of gastrointestinal bleeding,¹¹⁰ with the risk of major bleeding similar to that of ticagrelor and higher than that of clopidogrel.^{101,111-113} The HOST-EXAM study, with a mean age of 63.5 years, showed that long-term clopidogrel monotherapy significantly reduced the risk of all-cause death, nonfatal MI, stroke, readmission caused by ACS, and BARC type ≥ 3 bleeding events compared with aspirin monotherapy in DES-treated patients.¹⁰¹

A recent review summarized evidence for secondary prevention antiplatelet therapy for ACS patients aged ≥ 75 years, and concluded that in patients of high bleeding risk, antiplatelet monotherapy following short DAPT (1 to 3 months) may be associated with decreased bleeding complications and similar thrombotic events, as compared with standard 12-month DAPT.¹¹⁴ Clopidogrel seems to be the preferable P2Y₁₂ inhibitor caused by a better safety profile compared with a potent P2Y₁₂ inhibitor.

RECOMMENDATIONS.

- For elderly patients with ACS, DAPT should be given for 12 months (preferably aspirin in combination with clopidogrel). For patients with high bleeding risk, the duration of DAPT may be shortened to 1-3 months, followed by long-term monotherapy (preferably with clopidogrel).

COMBINED USE OF ORAL ANTICOAGULANT AGENT IN ATRIAL FIBRILLATION PATIENTS. The proportion of CAD patients combined with atrial fibrillation (AF) ranged between 6% and 21%.¹¹⁵ The combination of antiplatelet and oral anticoagulant (OAC) therapies is effective in reducing ischemic and thromboembolic events in these patients but increases the risk of bleeding.^{116,117} Therefore, the selection of optimal antithrombotic combinations has always been a clinical concern in these patients.

The adjunctive use of antiplatelet agents on OAC therapy resulted in an increased risk of bleeding compared with OAC monotherapy.¹¹⁸⁻¹²³ For such patients, it is recommended to assess the bleeding and ischemic risks using scoring tools. Currently, multiple RCTs (as shown in [Supplemental Table 4](#)) evaluating the efficacy and safety of different antithrombotic regimens in ACS patients combined with AF and/or PCI have demonstrated that the dual antithrombotic therapy with OAC plus P2Y₁₂ inhibitor (mainly clopidogrel) significantly reduced the risk of bleeding events and did not increase the risk of ischemic events compared with the traditional triple antithrombotic therapy with OAC plus DAPT.¹²⁴⁻¹³¹ However, a post hoc analysis of the AUGUSTUS (Open-Label, 2 × 2 Factorial, Randomized, Controlled Clinical Trial to Evaluate the Safety of

Apixaban vs Vitamin K Antagonist and Aspirin vs Aspirin Placebo in Patients With Atrial Fibrillation and Acute Coronary Syndrome and/or Percutaneous Coronary Intervention) study showed that continuing aspirin for more than 30 days in AF patients undergoing PCI increased bleeding risk without a significant reduction in ischemic events.¹³²

During the chronic phase in these cases, OAC monotherapy is recommended if there is no risk of high ischemic events.⁹² In the AFIRE (Atrial Fibrillation and Ischemic Events with Rivaroxaban in Patients with Stable Coronary Artery Disease) trial, 2,236 Japan AF patients treated with PCI or coronary artery bypass grafting (CABG) more than 1 year earlier (n = 1,697) or with documented CAD were randomized to receive either rivaroxaban monotherapy or combination therapy with rivaroxaban plus a single antiplatelet agent.¹³³ Rivaroxaban monotherapy was noninferior to combination therapy for efficacy and superior for major bleeding events in AF patients and stable CAD. The EPIC-CAD (Edoxaban versus Edoxaban with Antiplatelet Agent in Patients with Atrial Fibrillation and Chronic Stable Coronary Artery Disease) study included 1,040 South Korean AF patients with stable CAD, of which 524 patients were assigned to the edoxaban monotherapy group and 516 patients were assigned to the dual antithrombotic therapy group.¹³⁴ Edoxaban monotherapy led to a lower risk of a composite of death from any cause, MI, stroke, systemic embolism, unplanned urgent revascularization, or major or clinically relevant nonmajor bleeding at 12 months than dual antithrombotic therapy (HR: 0.44; 95% CI: 0.30-0.65; $P < 0.001$).

RECOMMENDATIONS. Refer to [Figure 5](#) for guidance.

- For CAD patients with AF undergoing PCI who have high bleeding risk or low ischemic risk, early cessation of aspirin (within 1 week postdischarge or until discharge from the hospital) should be considered. Afterward, dual therapy with an oral anticoagulant and a P2Y₁₂ receptor inhibitor (preferred by clopidogrel) for up to 6 months should be considered.
- For CAD patients with AF who have high ischemic and low bleeding risk, triple antithrombotic therapy including oral anticoagulant and DAPT can be maintained until 1 month after PCI. Afterward, dual therapy including an oral anticoagulant and a P2Y₁₂ inhibitor should be used for 12 months.
- During the chronic period, oral anticoagulant monotherapy is recommended for AF patients with stable CAD.

COMBINED NONCARDIAC ISCHEMIC STROKE/TRANSIENT ISCHEMIC ATTACK. Both CV and cerebrovascular

diseases share a similar pathological basis of atherosclerosis, and they are prone to develop simultaneously. CAD phenotype is documented in up to ~50% of patients with acute ischemic stroke.¹³⁵

Subgroup analyses of the CAPRIE study showed that clopidogrel monotherapy reduced the risk of ischemic events by up to 12.4% when compared with aspirin monotherapy in patients with multivascular lesions such as stroke and PAD.¹⁰⁰ The CHANCE (Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events) study included 5,170 patients with ischemic stroke/transient ischemic attack (TIA), 280 of whom had a history of CAD; the short-term (3 weeks) DAPT with clopidogrel plus aspirin followed by clopidogrel monotherapy was superior to aspirin monotherapy (HR: 0.68; $P < 0.001$).¹³⁶ On the other hand, the SOCRATES (Acute Stroke or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes) study, including 13,199 patients with a nonsevere ischemic stroke or high-risk TIA, showed that ticagrelor monotherapy failed to significantly reduce the primary endpoint events compared with aspirin monotherapy (6.7% vs 7.5%; HR: 0.89; 95% CI: 0.78-1.01; $P = 0.07$) in both Asian and non-Asian populations.¹¹²

Intracranial atherosclerotic stenosis (ICAS) is one of the crucial causes of acute and chronic ischemic cerebrovascular diseases. ICAS feature and poststroke hemorrhagic transformation are more common among East Asians than Caucasians (30%-50% and 15%-30%, respectively).¹³⁷⁻¹⁴⁰ These inherited conditions can contribute to the increased rates of ICH during antithrombotic therapy among the East Asian population. The SAMMPRIS (Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis) study confirmed that DAPT in ICAS patients was superior to DAPT in addition to interventional therapy.¹⁴¹ Therefore, the duration of DAPT in ICAS patients can be appropriately extended.

RECOMMENDATIONS.

- For ACS patients with a previous history of ischemic stroke or TIA, DAPT with clopidogrel plus aspirin for 12 months is recommended. If there is a high risk of ischemia, an appropriate extension of DAPT may be considered. If there is a high risk of bleeding or a history of hemorrhagic stroke, an appropriate shortening of DAPT may be considered.
- For patients with CCS, the following treatment regimens are recommended in case of a recent episode of ischemic stroke:
 - Within 24 hours of the onset of a minor stroke or high-risk TIA, treatment should be initiated

with DAPT of aspirin with clopidogrel for consecutive 21 days, followed by long-term antiplatelet monotherapy (preferred by clopidogrel).

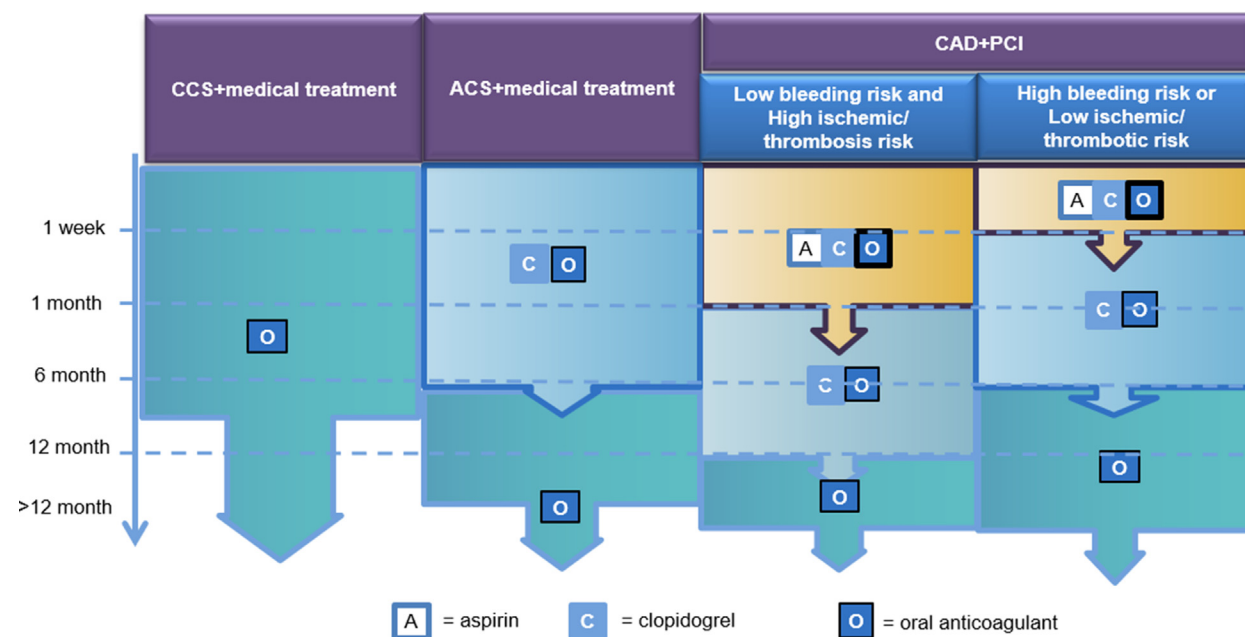
- For patients with symptomatic severe intracranial arterial stenosis within 30 days, treatment should be initiated with DAPT of aspirin with clopidogrel for 90 days, followed by long-term antiplatelet monotherapy (preferred by clopidogrel).

HEMORRHAGE OF THE DIGESTIVE TRACT. Hemorrhage of the digestive tract is the most common bleeding complication during long-term antiplatelet therapy.¹⁴² Consensus from multidisciplinary experts concurred on the clinical features that constituted HBR of digestive tracts, which include a history of gastrointestinal ulcer or bleeding; long-term use of nonsteroidal anti-inflammatory drugs or glucocorticoids; or ≥ 2 risk factors (age ≥ 65 years, dyspepsia, gastroesophageal reflux disease, helicobacter pylori infection, or long-term alcohol consumption).¹⁴³ Therefore, for patients with HBR of the digestive tract, special attention should be paid to balance the risks of ischemia and hemorrhage of the digestive tract treated with antiplatelet therapy.

Several studies showed that clopidogrel monotherapy significantly reduced the adverse reactions of the digestive tract after long-term treatment when compared with aspirin.^{101,144} According to the analysis of bleeding events in the PLATO study, it was found that compared with clopidogrel, ticagrelor increased the incidence of spontaneous gastrointestinal hemorrhage during the course of DAPT in patients with ACS ($P = 0.048$).¹⁴⁵

There is very limited evidence for interruption or resumption of antiplatelet therapy for patients with hemorrhage of the digestive tract. In a prospective study, 156 Chinese patients with peptic ulcer bleeding after endoscopic hemostasis treatment were randomized to receive treatment with low-dose aspirin 80 mg/d ($n = 78$) or placebo ($n = 78$) for 8 weeks.¹⁴⁶ The results showed that recurrence rates of ulcer bleeding within 30 days were 10.3% and 5.4% in the aspirin and placebo groups, respectively. All-cause mortality within 8 weeks was 1.3% and 12.9%, respectively. Mortality from CV, cerebrovascular, or gastrointestinal complications was lower in the low-dose aspirin group than in the placebo group (1.3% vs 10.3%), suggesting that maintaining aspirin therapy may increase the risk of recurrent bleeding but may decrease mortality. A retrospective study included 102 Canadian AMI patients who subsequently developed ulcer bleeding during

FIGURE 5 Antithrombotic Strategy for Atrial Fibrillation Patients Combined With CAD



It is recommended to assess the bleeding and ischemic risks for patients receiving adjunctive use of antiplatelet agents on oral anticoagulant (OAC) therapy. During the chronic phase in these cases, OAC monotherapy is recommended if there is no risk of high ischemic event. ACS = acute coronary syndrome; CAD = coronary artery disease; CCS = chronic coronary syndrome; PCI = percutaneous coronary intervention.

hospitalization.¹⁴⁷ A total of 64 patients interrupted aspirin while 38 patients continued, with similar 30-day rates for both further bleeding and mortality between the 2 groups. Given the fact that antiplatelet therapy has been the cornerstone treatment of CAD,^{4,6,8,92,148,149} after endoscopic hemostasis therapy, re-administration of aspirin or P2Y₁₂ inhibitors is recommended.¹⁵⁰⁻¹⁵²

RECOMMENDATIONS.

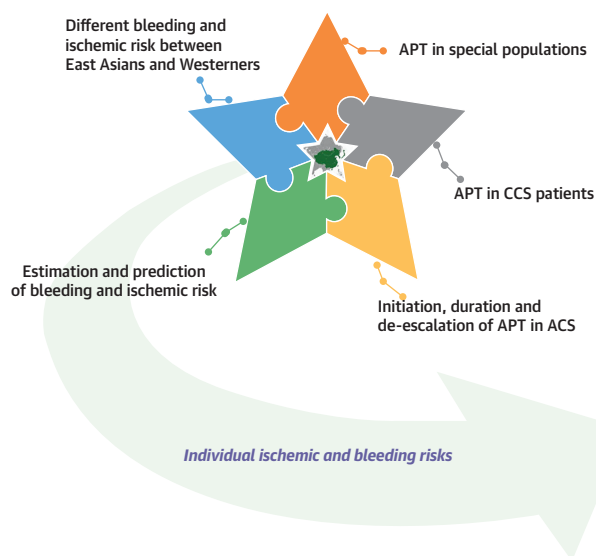
- Coadministration of PPI in the first 6 months of dual antiplatelet therapy may be considered for patients with a high risk of hemorrhage of the digestive tract, whereas prophylactic PPI use is not recommended for patients at low risk.
- If there is apparent bleeding during DAPT, antiplatelet therapy interruption may be considered. Once the condition is stabilized, antiplatelet therapy should be resumed as soon as possible.

COMBINED CKD. CKD is a common comorbidity in patients with ACS. According to a U.S. survey, 30.5% of patients with STEMI and 42.9% of patients with non-STEMI had CKD phenotype as a comorbidity.¹⁵³ A cohort study in China suggested that the prevalence of moderate to severe renal insufficiency in patients with non-ST-segment elevation ACS was 11.6% to 22.4%.¹⁵⁴ CKD is a major risk factor for CVD: as

estimated glomerular filtration rate (eGFR) declines below 60~75 mL/min/1.73 m², the probability of developing CAD increases linearly.¹⁵⁵ Risks of major bleeding and ischemic events increase in advanced CKD patients.^{155,156}

Limited evidence exists to guide antiplatelet therapy in CKD patients undergoing PCI. In the CURE study, more than one-quarter of patients had impaired renal function. DAPT with clopidogrel plus aspirin significantly reduced the risk of CV death than aspirin monotherapy without an increase in the incidence of major bleeding.¹⁵⁷ The SWEDEHEART registry (n = 36,001) showed 20.4% incidence of renal insufficiency (eGFR ≤60 mL/min/1.73 m²). DAPT with clopidogrel plus aspirin for 12 months significantly reduced the endpoint events of death/ischemic stroke or reinfarction in CKD patients, compared with DAPT for 3 months.¹⁵⁸ The EPICOR Asia (long-term follow-up of antithrombotic management patterns in acute Coronary syndrome patients) study showed that early interruption of antiplatelet treatment was possibly associated with an increased risk of adverse ischemic events in patients with severe CKD.¹⁵⁹ The TRANSLATE-ACS (Treatment with ADP Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome) study (11,108 PCI-treated patients) demonstrated that the risk of

CENTRAL ILLUSTRATION Updated Recommendations on Antiplatelet Therapy for East Asian CAD Patients



• East Asian patients have a higher risk of bleeding than Western patients.

• Risk stratification based on bleeding and ischemia risks in East Asia. Low body weight, frailty, HF, and PAD are additional risk factors for HBR compared to western guidelines. AF, HF, and anemia are additional risk factors for high ischemic risk compared to western guidelines.

• Maintain DAPT for 12 months for ACS, (3-6 months of DAPT in cases of HBR), and long-term (>12 months) DAPT is not generally recommended.

• For ACS patients initially receiving aspirin with ticagrelor or prasugrel, active de-escalated to aspirin with clopidogrel after 1 month.

• For patients with aspirin intolerance or high bleeding risk, DAPT with indobufen can be chosen as an alternative to DAPT with aspirin.

• CAD patients requiring DAPT can initiate treatment with a fixed-dose combination.

• For CCS patients with HBR undergoing PCI, antiplatelet monotherapy with clopidogrel after 1-3 months of DAPT can be considered.

• Maintenance of antiplatelet monotherapy with clopidogrel or aspirin is recommended for CCS patients.

• APT in special populations: elderly population, combined use of oral anticoagulant agent, combined non-cardiac ischemic stroke/TIA, hemorrhage of digestive tract, combined CKD, and after CABG.

Gong Y, et al. JACC Asia. 2025;5(7):821-846.

This updated consensus emphasized different bleeding and ischemic risks between East Asian and Western patients first. Then, the following topics are discussed: bleeding and ischemic risk estimation and prediction, initiation and duration, and de-escalation of dual antiplatelet therapy (DAPT) in acute coronary syndrome (ACS) patients, antiplatelet therapy (APT) in chronic coronary syndrome (CCS) patients, and APT in special populations. Different content of this consensus compared with Western guidelines were highlighted with red words. AF = atrial fibrillation; CABG = coronary artery bypass grafting; CKD = chronic kidney disease; HBR = high bleeding risk; HF = heart failure; PAD = peripheral artery disease; TIA = transient ischemic attack.

moderate or severe bleeding increases according to the severity of CKD during ticagrelor or prasugrel treatment, and that patients with severe CKD (stage ≥ 4) were more likely to have their antiplatelet treatment interrupted or switched to clopidogrel, and early bleeding events may be the primary cause for interruption.¹⁶⁰ In ACS patients treated with concomitant ARB, there was a significant increase in serum creatinine increased $>50\%$, kidney-associated adverse events and kidney function-related adverse events for patients receiving ticagrelor compared with clopidogrel.¹⁶¹ The COAPT (Canadian Observational Antiplatelet Study) included 1,921 patients with available information regarding eGFR, of which 14.3% had eGFR ≤ 60 mL/min/1.73 m². The results showed that the increased risk of bleeding was only observed in ACS patients on treatment with prasugrel/ticagrelor ($P = 0.007$), while not in subjects on treatment with clopidogrel ($P = 0.64$).¹⁶² Taken together, clopidogrel may be a safer treatment for ACS patients with severe CKD.

A meta-analysis (5 randomized trials; 1,902 patients with CKD) demonstrated the efficacy and

safety of DAPT according to treatment duration in CKD patients. Short DAPT (≤ 6 months) was associated with a similar incidence of ischemic events, compared with 12-month DAPT (RR: 0.93; 95% CI: 0.64-1.36; $P = 0.72$). 12-month DAPT was also associated with a similar incidence of the primary outcome compared with extended DAPT (≥ 30 months) (RR: 1.04; 95% CI: 0.67-1.62; $P = 0.87$). Numerically lower major bleeding event rates were detected with short vs 12-month DAPT (RR: 0.69; 95% CI: 0.30-1.60; $P = 0.39$) and 12-month vs extended DAPT (RR: 0.83; 95% CI: 0.35-1.93; $P = 0.66$) in these patients.¹⁶³ Short DAPT does not appear to be inferior to longer DAPT in CAD patients with CKD.

RECOMMENDATIONS.

- For CAD patients undergoing PCI with renal insufficiency, DAPT of aspirin with a P2Y₁₂ inhibitor (preferred by clopidogrel) for 6-12 months is reasonable.
- If concomitant ARB therapy is required, clopidogrel plus aspirin is the preferred DAPT regimen in CAD patients with moderate or severe CKD.

ANTIPLATELET TREATMENT FOLLOWING CABG.

CABG is recommended in ACS patients with patent IRA and anatomy unsuitable for PCI, and either a large myocardial area in jeopardy.⁸ Several studies compared different DAPT combinations with aspirin alone with mixed results.¹⁶⁴ In a retrospective registry (18,069 patients undergoing CABG), DAPT with clopidogrel plus aspirin showed a lower incidence of ischemic events at 6 months (HR: 0.65; 95% CI: 0.55-0.77; $P < 0.001$) with similar incidence of major bleeding (HR: 1.11; 95% CI: 0.69-1.78) compared with aspirin alone.¹⁶⁵ Meanwhile, 2,072 patients with ACS in the CURE study received CABG surgery, of whom 1,061 and 1,011 patients were randomized to receive either aspirin alone or DAPT with clopidogrel plus aspirin. DAPT vs aspirin monotherapy reduced the risk of ischemic events by 11% but increased the risk of bleeding complications by 30%.¹⁶⁶ The DACAB (Different Antiplatelet Therapy Strategy After Coronary Artery Bypass Graft Surgery) trial (500 Chinese patients undergoing CABG) randomized patients to receive ticagrelor plus aspirin, ticagrelor alone, or aspirin alone during 12 months within 24 hours post-CABG. DAPT with ticagrelor plus aspirin significantly increased saphenous vein graft patency (88.7% vs 76.5%; absolute difference, 12.2%; 95% CI: 5.2%-19.2%; $P < 0.001$) compared with aspirin alone, with a few incidences of major bleeding in each group.¹⁶⁷ However, the POPular-CABG trial ($n = 499$) showed no significant difference in 1-year saphenous vein graft patency between DAPT with aspirin plus ticagrelor and aspirin alone.¹⁶⁸ Subgroup analysis focusing on CABG cohorts of the PLATO¹⁶⁹ and TRITON-TIMI 38¹⁷⁰ trials were all in line with the whole set. In the CABG cohorts of the PLATO ($n = 1,261$),¹⁶⁹ the relative reduction of the primary composite endpoint of CV death, myocardial infarction, or stroke at 12 months (10.6% with ticagrelor vs 13.1% with clopidogrel; HR: 0.84; 95% CI: 0.60-1.16; $P = 0.29$) was consistent with the results of the whole trial. Total mortality was reduced from 9.7% to 4.7% (HR: 0.49; 95% CI: 0.32-0.77; $P < 0.01$), and CV death from 7.9% to 4.1% (HR: 0.52; 95% CI: 0.32-0.85; $P < 0.01$). There was no significant difference in CABG-related major bleeding between the randomized treatments. A subset of the TRITON TIMI 38 study,¹⁷⁰ where patients with ACS were randomized to treatment with aspirin and either clopidogrel or prasugrel, underwent isolated CABG ($n = 346$). A significantly higher 12-hour blood loss from chest tube (655 ± 580 mL vs 503 ± 378 mL; $P = 0.050$) was observed with prasugrel compared with clopidogrel, without significant differences in red blood cell transfusion (2.1 U vs 1.7 U; $P = 0.442$) or the total

donor exposure (4.4 units vs 3.0 units; $P = 0.463$). All-cause mortality at 30 days was significantly reduced with prasugrel (2.31%) compared with 8.67% with clopidogrel (OR: 0.26; $P = 0.025$).

RECOMMENDATIONS.

- If patients presenting with ACS stop DAPT to undergo CABG, it is recommended that they resume DAPT including clopidogrel or ticagrelor after surgery and maintain for at least 12 months.

COMPLIANCE OF ANTIPLATELET THERAPY IN EAST ASIAN PATIENTS

Compliance with medication is strongly associated with the prognosis. East Asian patients face challenges in adhering to antiplatelet therapy caused by economic concerns, a high incidence of adverse events, and limited information about the drug's effects.^{171,172} In subjects who are noncompliant with DAPT caused by bleeding, the 2-year risk of MACE was increased by 50% compared with compliant subjects.¹⁷³

Multiple factors affect compliance with antiplatelet therapy, including treatment factors, socioeconomic factors, patient factors, and so on.¹⁷⁴⁻¹⁷⁶ Among these, adverse reactions and convenience of medication are common factors in drug discontinuation.^{106,177-180} Comprehensive interventions—such as patient education—can increase treatment compliance.¹⁸¹ The complexity of treatment regimens and the large number of concomitant medications are the 2 main barriers to compliance with treatment after discharge. The use of antiplatelet fixed-dose combination (FDC) can reduce the number of pills taken by patients, thereby reducing their drug burden.¹⁸² The SECURE (Secondary Prevention of Cardiovascular Disease in the Elderly) study (2,499 patients with MI within the previous 6 months) showed that medication adherence was higher in the FDC group (aspirin, ramipril, and atorvastatin) than in the usual-care group. The relative risk of the MACE was also significantly reduced in the FDC group (9.5% vs 12.7% during follow-up for a median of 36 months; HR: 0.76; 95% CI: 0.60-0.96; $P = 0.02$).¹⁸⁰ Western large-scale database (26,834 Italian patients presented with ACS) showed that compliance with clopidogrel/aspirin FDC was significantly higher than that with separate DAPT (81.5% vs 72.9%).¹⁸³

During antiplatelet therapy, the East Asian population has a higher risk of serious bleeding compared with the Western population. A recent meta-analysis (2 trials including 17,003 East Asians and 9 trials including 117,457 Western participants) demonstrated that low-dose aspirin (≤ 100 mg once daily) for

primary prevention showed a similar effect in reducing the MACE rate (RR of East Asians: 0.87; 95% CI: 0.71-1.05; RR of Westerners: 0.90; 95% CI: 0.85-0.95) ($P_{interaction} = 0.721$) and increased risk of major bleeding (RR of East Asians: 2.48; 95% CI: 1.86-3.30; RR of Westerners: 1.45; 95% CI: 1.26-1.66) ($P_{interaction} = 0.001$).¹⁸⁴ The East Asian population has unique pharmacokinetic and pharmacodynamics profiles during potent P2Y₁₂ inhibitors.¹⁰ East Asians exhibit 30% to 47% higher levels of prasugrel's active metabolites compared with Caucasians. In addition, the exposure to ticagrelor and its major active metabolite (AR-C124910XX) is increased by approximately 40% and 48%, respectively, in East Asians compared with Caucasians. In the TWILIGHT trial, the incidence of dyspnea-related ticagrelor discontinuation was 6.4% and 9.1% at 3 and 15 months after PCI, respectively. This discontinuation tended to occur earlier rather than late after PCI, and several demographic and clinical conditions (eg, race, smoking, PAD, obesity, and older age) predicted its occurrence.¹⁸⁵ A cohort study evaluated the incidence of questionnaire-based adverse events and its association with the type and effect of P2Y₁₂ inhibitors in East Asian patients presented with ACS undergoing PCI (n = 944). During the 1-month follow-up, DAPT with ticagrelor showed higher risks of bleeding (any BARC type: 45.6% vs 23.6%; OR: 2.71) and dyspnea (26.3% vs 13.6%; OR: 2.25) compared with DAPT with clopidogrel. During 1-year follow-up, DAPT with ticagrelor showed a higher risk of premature discontinuation compared with DAPT with clopidogrel (27.8% vs 4.7%; HR: 8.84), which risk appeared frequent during the first month (14.4%) during DAPT with ticagrelor. Early occurrence of bleeding and dyspnea synergistically increased the risk of DAPT non-adherence, irrespective of the type of P2Y₁₂ inhibitor.¹⁸⁶

RECOMMENDATIONS.

- CAD patients requiring DAPT can initiate treatment with a fixed-dose combination.
- Fixed-dose combination treatment can improve patient compliance and can be routinely applied for 12 months with extending or shortening its

prescription duration based on the risk of ischemia and bleeding.

HIGHLIGHTS AND CONCLUSIONS

The standardization of antiplatelet therapy in patients with CAD is essential for reducing CV events. This updated consensus summarizes recent clinical and research evidence from East Asian countries and provides detailed recommendations tailored for East Asian patients (**Central Illustration**). "East Asian Paradox" was emphasized. There were both similarities and differences compared with Western consensus or guidelines. The biggest difference is that our consensus did not support use of long-term maintenance (>12 months) of DAPT even in ACS patients with high ischemic risk and support active de-escalation of DAPT. With the release of multiple clinical studies, many critical problems related to the standardization of antiplatelet therapy in the East Asian population have been solved, and the treatment regimen has become increasingly normative. However, several problems still remain, and many clinical studies in the East Asian population are currently ongoing to resolve these issues (**Supplemental Table 5**). It is expected that these studies will be helpful in exploring the optimal antiplatelet strategy in the near future for East Asian patients with CAD characterized by different clinical manifestations.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS antiplatelet therapy, bleeding, compliance, coronary artery disease, de-escalation, East Asia

APPENDIX For supplemental tables, please see the online version of this paper.