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Mini-Review

Low-Dose Aspirin in Coronary Artery Disease: Evidence and Implications

Wen Zheng[1], Zhao-Ting Gong[1], Xin Li[1], Hai-Yan Qian[1*]

Department of Cardiology, Center for Coronary Artery Disease, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China

ABSTRACT

Aspirin remains cornerstone therapy for coronary artery disease secondary prevention, yet optimal dosing is debated, particularly in East Asian populations demonstrating heightened bleeding risk with standard antiplatelet regimens. This mini-review evaluates low-dose aspirin (≤50 mg) by synthesizing pharmacological mechanisms and clinical evidence. Pharmacokinetic studies demonstrate presystemic portal metabolism enabling selective platelet Cyclooxygenase-1 (COX-1) inhibition while preserving endothelial prostacyclin synthesis. Pharmacodynamic data suggest 50 mg as the minimum dose achieving >90% thromboxane suppression with preserved prostacyclin synthesis, whereas 30-40 mg produces incomplete inhibition (77-85%) with high inter-patient variability. Since platelets lack nuclei and cannot synthesize new COX-1 after acetylation, steady-state inhibition exceeding 95% occurs within 7-10 days of daily 50 mg dosing. Clinical evidence remains limited to small trials (N=100-948), none adequately powered for cardiovascular endpoints. The CABADAS trial demonstrated 50 mg aspirin efficacy post-Coronary Artery Bypass Grafting (CABG) with lowest clinical event rates (13.9% vs 20% for aspirin plus dipyridamole and 16.9% for anticoagulation). A recent propensity-matched cohort showed similar cardiovascular outcomes but significantly reduced bleeding with 50 mg vs. 100 mg in elderly Chinese patients (Hazard Ratio (HR) 1.671, p=0.040). The ongoing LEAST trial (N=3,612) represents the first large-scale Randomized Controlled Trial (RCT) comparing reduced-dose vs standard-dose aspirin in East Asian ST-segment Elevation Myocardial Infarction (STEMI) patients undergoing Percutaneous Coronary Intervention (PCI) receiving contemporary Dual Antiplatelet Therapy (DAPT), with results expected in 2027-2028. Current international guidelines universally recommend 75-100 mg based on extensive Western trial data. While pharmacological principles and observational data suggest potential benefits of lower doses in high bleeding East Asian patients, definitive randomized trial evidence is required before routine implementation.

Key words

Aspirin; Coronary artery disease; Pharmacology; East Asian; Bleeding risk; Personalized medicine

INTRODUCTION

Aspirin's irreversible platelet COX-1 inhibition has established it as cornerstone therapy for Coronary Artery Disease (CAD) prevention [1]. Current international guidelines (2025 ACC/AHA and 2023 ESC) recommend 75-100 mg daily (Class I, Level A) for secondary prevention, based predominantly on Western population trials [2,3]. The Antithrombotic Trialists' Collaboration demonstrated that aspirin reduces serious vascular events by approximately 22% in high-risk patients (odds ratio 0.78, 95% Confidence Interval (CI) 0.73-0.84), with efficacy established in the 75-150 mg dose range4.

East Asian populations present a paradoxical profile challenging conventional dosing: Lower baseline platelet reactivity yet higher bleeding complications with standard antiplatelet regimens [5,6]. The Korean HOST-EXAM study demonstrated clopidogrel

Correspondence to: Hai-Yan Qian, Department of Cardiology, Center for Coronary Artery Disease, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China, E-mail: ahqhy712@163.com

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monotherapy superiority over 100 mg aspirin monotherapy for long-term maintenance after completing DAPT (HR 0.73, 95% CI 0.59-0.90 for Major Adverse Cardiovascular And Cerebrovascular Events (MACCE)), suggesting that alternative antiplatelet strategies may be preferable for some East Asian patients [7]. This has prompted interest in low-dose aspirin (≤50 mg) to maintain efficacy while reducing bleeding risk.

Despite biological plausibility and increasing clinical use, particularly in East Asian populations, very low doses (<75 mg) lack adequate clinical trial evidence for cardiovascular endpoints. This mini-review synthesizes pharmacological understanding, evaluates clinical data, and examines ongoing investigations to address whether low-dose aspirin represents rational personalized therapy or potentially inadequate treatment.

Pharmacological mechanisms

Aspirin's unique pharmacology fundamentally underlies its dose-dependent selectivity. Pedersen and FitzGerald's seminal 1984 study demonstrated approximately 40-50% oral bioavailability with substantial presystemic hepatic metabolism8. Critically, following 20 mg oral administration, serum thromboxane B_2 decreased 39% before aspirin appeared in peripheral plasma, demonstrating presystemic platelet inhibition. Orally absorbed aspirin enters portal circulation before systemic distribution, exposing platelets to high local concentrations achieving complete COX-1 acetylation. Subsequent hepatic metabolism reduces systemic levels, relatively preserving vascular endothelial Prostacyclin (PGI2) synthesis [8].

Dose-response relationships have been extensively characterized. Very low doses (10-30 mg) demonstrate insufficient effects. Weksler showed 10mg produced only 61% platelet thromboxane inhibition without bleeding time prolongation [9]. Studies of 30mg doses have demonstrated variable and incomplete platelet inhibition. While partial effects may be observed in stable patients, these lower doses lack the consistency required for reliable antiplatelet therapy, particularly during acute coronary syndromes.

The 40mg dose has been extensively studied. Daily 40 mg produced approximately 85% serum thromboxane inhibition but only 42% urinary 11-dehydro-thromboxane suppression, indicating incomplete systemic inhibition10. Importantly, 40 mg demonstrated minimal or no prostacyclin inhibition, whereas higher doses (320-1280 mg) significantly suppressed PGI2 synthesis. FitzGerald demonstrated 40 mg inhibited approximately 77% serum thromboxane with only 35% aortic prostacyclin inhibition, compared to 325 mg producing 99% thromboxane but 75% prostacyclin inhibition [11].

Multiple studies establish 50 mg as the minimum dose achieving substantial, reliable inhibition. Clarke's 1991 study showed 50 mg controlled-release aspirin produced substantial platelet function inhibition and thromboxane suppression without significant prostacyclin inhibition, while <50 mg caused incomplete effects [12]. Patrick's 2015 modeling calculated inhibitory dose-50 (ID50) as 49.9 mg, with maximum thromboxane inhibition of 98.9% [13]. Since platelets lack nuclei and cannot synthesize new COX-1 after acetylation, and daily platelet turnover approximates 10%, steady-state inhibition exceeding 95% occurs within 7-10 days of daily 50 mg dosing [14].

Pharmacological data suggest 50 mg as the minimum dose likely to achieve >90% thromboxane suppression with preserved prostacyclin synthesis, while 30-40 mg demonstrates incomplete, variable inhibition potentially inadequate during acute coronary syndromes when enhanced platelet activation may overwhelm partial COX-1 inhibition.

Clinical evidence

Clinical trial evidence for low-dose aspirin remains strikingly limited. Berent et al. study compared 50 mg vs 100 mg in 100 CAD patients over 5 years, finding no differences in antiplatelet response or cardiovascular events, but was severely underpowered [15].

The CABADAS trial (1991) represents the largest completed study, randomizing 900 CABG patients to 50 mg aspirin, 50 mg plus dipyridamole, or anticoagulation. 1 year vein graft patency was similar across groups. Distal anastomosis occlusion rates were 15% for aspirin, 11% for aspirin plus dipyridamole, and 13% for anticoagulation. Clinical event rates were 13.9% for aspirin alone, 20.3% for aspirin plus dipyridamole, and 16.9% for anticoagulation, demonstrating aspirin monotherapy had the lowest event rate [16]. While supporting 50 mg efficacy post-CABG, generalizability to medical populations remains uncertain.

Wang et al. propensity-matched cohort compared 50 mg vs. 100 mg in 426 elderly Chinese patients, finding similar Major Adverse Cardiovascular Events (MACE) rates (6.35 vs. 6.65 events/100 patient-years, HR 0.921, 95% CI 0.399-2.127, P=0.848) but significantly higher bleeding with 100 mg (28.34 *vs.* 17.25 events/100 patient-years, HR 1.671, 95% CI 1.024-2.712, p=0.040). However, the observational design and non-randomized dose selection introduce substantial selection bias [17].

The low-dose evaluation of Aspirin in STEMI patients undergoing PCI (LEAST) trial addresses this critical evidence gap. The published protocol describes a multicenter, double-blind RCT enrolling 3612 STEMI patients across 34 Chinese centers [18]. Eligible patients aged 18-80 undergoing PCI receive low-dose vs. standard maintenance aspirin, all with concomitant ticagrelor. Primary endpoint is 12-month MACE (cardiovascular death, Myocardial Infarction (MI), stroke); secondary endpoints include Bleeding Academic Research Consortium (BARC) bleeding and stent thrombosis. Recruitment began July 2025, completing December 2026, with results expected in 2027-2028.

LEAST's significance is paramount as the first adequately powered RCT directly addressing whether low-dose aspirin provides non-inferior cardiovascular protection in acute STEMI in the contemporary DAPT era. The 3612-patient sample provides statistical power for non-inferiority assessment in East Asian patients most likely to benefit from dose reduction.

Results will definitively inform whether low-dose aspirin represents appropriate personalization or inadequate therapy.

The 2025 ACC/AHA and 2023 ESC guidelines both recommend 75-100 mg (Class I, Level A), based on extensive Western trials. Despite this, low-dose aspirin (50 mg) is increasingly prescribed in clinical practice, reflecting clinician judgment for high bleeding-risk, elderly, or low-weight patients. This creates substantial tension between evidence-based guidelines and real-world practice.

The east asian paradox and clinical implications

East Asian populations demonstrate lower baseline platelet reactivity yet paradoxically higher bleeding complications with standard antiplatelet doses [5,6]. Multiple mechanisms may contribute: Higher prevalence of CYP2C19 loss-of-function alleles (50-60% *vs.* 25-30% in Europeans) which primarily affects clopidogrel metabolism [19], ethnic variation in COX-1 polymorphisms, lower body mass index (23-25 *vs* 27-30 kg/m2) [20] ,and higher dietary omega-3 intake.

HOST-EXAM's demonstration that clopidogrel monotherapy outperformed 100 mg aspirin monotherapy in 5438 Korean patients (HR 0.73 for MACCE) suggests that alternative antiplatelet strategies may be preferable in specific clinical contexts [7]. However, important caveats exist: The paradox is not universally accepted, bleeding definitions vary across trials, and findings may not generalize uniformly across Chinese, Japanese, and Korean populations.

If LEAST demonstrates non-inferiority, several populations might benefit from low doses: high bleeding-risk, low body weight patients, and chronic kidney disease patients. Future personalized strategies may integrate bleeding/ischemic risk scores [21], genetic testing, and platelet function monitoring. However, these approaches require prospective validation. Previous platelet function testing trials (GRAVITAS, TRIGGER-PCI) failed to demonstrate benefit [22,23].

Critical research priorities extend beyond LEAST: NSTEMI, unstable angina, and stable CAD populations all lack adequately powered low-dose trials. Long-term efficacy over decades-long treatment courses requires investigation. Combination therapy with different P2Y12 inhibitors needs specific study, and biomarker development might identify patients benefiting from dose reduction.

Current recommendations pending LEAST results: Follow guideline-recommended 75-100 mg for most patients. Consider 50 mg only in exceptional circumstances with full patient disclosure of evidence limitations and close monitoring. Post-LEAST practice depends on results-if non-inferior, update guidelines for East Asian STEMI patients; if inferior, clearly establish inadequate protection; if inconclusive, recognize need for additional research.

CONCLUSION

Low-dose aspirin presents a compelling yet unproven therapeutic strategy. While pharmacological principles support potential efficacy, clinical evidence remains insufficient to justify routine implementation. The ongoing LEAST trial will provide the first adequately powered randomized assessment, with results expected in 2027-2028. Until definitive evidence emerges, clinicians should follow guideline-recommended 75-100 mg doses, reserving lower doses only for exceptional circumstances with appropriate patient counseling. The aspirin dosing debate exemplifies personalized medicine's fundamental challenge: Balancing biological plausibility with rigorous clinical evidence to optimize individual patient outcomes while ensuring population-level safety.

REFERENCES

1. Patrono C, Baigent C. Nonsteroidal anti-inflammatory drugs and the heart. Circulation. 2014;129:907-916.
2. Rao SV, O'Donoghue ML, Ruel M, Rab T, Tamis-Holland JE, Alexander JH, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2025;85:2225-2237.
3. ESC Scientific Document Group.2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023;44:3720-3826.
4. Trialists' Collaboration A. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction and stroke in high risk patients. BMJ. 2002;324:71-86.
5. Kang J, Kim HS. The evolving concept of dual antiplatelet therapy after percutaneous coronary intervention: focus on unique feature of East Asian and "Asian Paradox". Korean Circ J. 2018;48:537-551.
6. Levine GN, Jeong YH, Goto S, Anderson JL, Huo Y, Mega JL, et al. Expert consensus document: World Heart Federation expert consensus statement on antiplatelet therapy in East Asian patients with ACS or undergoing PCI. Nat Rev Cardiol. 2014;11:597.
7. Kang J, Park KW, Lee H, Hwang D, Yang HM, Rha SW, et al. Aspirin versus clopidogrel for long-term maintenance monotherapy after percutaneous coronary intervention: the HOST-EXAM extended study. Circulation. 2023;147:108-117.
8. Pedersen AK, FitzGerald GA. Dose-related kinetics of aspirin: presystemic acetylation of platelet cyclooxygenase. N Engl J Med. 1984;311:1206-1211.
9. Weksler BB, Pett SB, Alonso D, Richter RC, Stelzer P, Subramanian V, et al. Differential inhibition by aspirin of vascular and platelet prostaglandin synthesis in atherosclerotic patients. N Engl J Med. 1983;308:800-805.
10. Patrono CA, Ciabattoni G, Patrignani PA, Pugliese FR, Filabozzi PA, Catella FR, et al. Clinical pharmacology of platelet cyclooxygenase inhibition. Circulation. 1985;72:1177-1184.
11. FitzGerald GA, Oates JA, Hawiger JA, Maas RL, Roberts LJ, Lawson JA, et al. Endogenous biosynthesis of prostacyclin and thromboxane and platelet function during chronic administration of aspirin in man. J Clin Invest. 1983;71:676-688.
12. Clarke RJ, Mayo G, Price P, FitzGerald GA. Suppression of thromboxane A2 but not of systemic prostacyclin by controlled-release aspirin. N Engl J Med. 1991;325:1137-1141.
13. Patrick J, Dillaha L, Armas D, Sessa WC. A randomized trial to assess the pharmacodynamics and pharmacokinetics of a single dose of an extended-release aspirin formulation. Postgrad Med. 2015;127:573-580.
14. Patrignani P, Filabozzi P, Patrono C. Selective cumulative inhibition of platelet thromboxane production by low-dose aspirin in healthy subjects. J Clin Invest. 1982;69:1366-1372.

15. Berent R, Auer J, Franklin B, Schmid P, von Duvillard SP. Platelet response to aspirin 50 and 100 mg in patients with coronary heart disease over a five-year period. Am J Cardiol. 2011;108:644-650.
16. van der Meer J, Hillege HL, van Gilst WH, Lie KI, Kootstra GJ, Ascoop CA, et al. Prevention of one-year vein-graft occlusion after aortocoronary-bypass surgery: a comparison of low-dose aspirin, low-dose aspirin plus dipyridamole, and oral anticoagulants. The Lancet. 1993;342:257-264.
17. Wang X, Wang H, Zheng Q, Geng H, Zhang J, Fan Y, et al. Outcomes Associated with 50 mg/d and 100 mg/d aspirin for the prevention and management of cardiovascular disease in Chinese elderly: single-center interim analysis of a multicenter, prospective, observational study. Int J Gen Med. 2022;15:7089.
18. Zheng W, Gong ZT, Qian HY. Study protocol for low-dose evaluation of aspirin in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention (LEAST): a multicenter, double-blind, randomized controlled clinical trial. Ann Med. 2025;57:2589577.
19. Scott SA, Sangkuhl K, Stein CM, Hulot JS, Mega JL, Roden DM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. Clin Pharmacol Ther. 2013;94:317-323.
20. Tan KC. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004.
21. Costa F, Van Klaveren D, James S, Heg D, Räber L, Feres F, et al. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. Lancet. 2017;389:1025-1034.
22. Price MJ, Berger PB, Teirstein PS, Tanguay JF, Angiolillo DJ, Spriggs D, et al. Standard-vs high-dose clopidogrel based on platelet function testing after percutaneous coronary intervention: the GRAVITAS randomized trial. JAMA. 2011;305:1097-2105.
23. Trenk D, Stone GW, Gawaz M, Kastrati A, Angiolillo DJ, Müller U, et al. A randomized trial of prasugrel versus clopidogrel in patients with high platelet reactivity on clopidogrel after elective percutaneous coronary intervention with implantation of drug-eluting stents: results of the TRIGGER-PCI (Testing Platelet Reactivity In Patients Undergoing Elective Stent Placement on Clopidogrel to Guide Alternative Therapy With Prasugrel) study. J Am Coll Cardiol. 2012;59:2159-2164.