



Aspirin Resistance in Coronary Artery Disease: Prevalence and Clinical Implications

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Received: September 18, 2025

Accepted: October 13, 2025

ePublished: June 6, 2026

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Citation: Dolikhani M, Shakibamaram G, Karami M, Barati A, Sabzghabaei A. Aspirin resistance in coronary artery disease: prevalence and clinical implications. J Emerg Pract Trauma 2025;11(1):27-32. doi:10.34172/jept.1777

Abstract

Introduction: Coronary artery disease (CAD) remains a major cause of morbidity and mortality worldwide. Aspirin is a cornerstone in CAD management due to its antiplatelet effects; however, aspirin resistance can lead to suboptimal outcomes. In Iran, limited data exist regarding the prevalence of aspirin resistance among patients presenting with chest pain. This study aimed to determine the prevalence of aspirin resistance and its clinical implications in a cohort of Iranian patients with CAD.

Methods: This prospective cross-sectional study was conducted in 2021 at the Emergency Department of Imam Hossein Hospital, Tehran, Iran. A total of 155 patients aged ≥ 18 years on daily aspirin therapy (≥ 75 mg for ≥ 7 days) were recruited using convenience sampling. Bleeding time was measured by the standard SimPlate method (resistance defined as $BT < 5$ minutes). Normality of variables was tested with the Shapiro-Wilk test; between-group comparisons were performed using the *t*-test for continuous variables and the χ^2 test for categorical variables. Statistical significance was defined as $P < 0.05$.

Results: Among 155 participants (mean age 57.49 ± 13.13 years; 59.4% male), 133 (85.8%) exhibited aspirin resistance. Resistant patients were significantly older than sensitive ones (59.64 ± 12.47 vs. 44.50 ± 9.05 years; $P < 0.001$). No gender difference was observed ($P = 0.363$). Compared with aspirin-sensitive patients, resistant patients had higher rates of hypertension (42.1% vs. 18.2%; $P = 0.033$), diabetes mellitus (42.9% vs. 9.1%; $P = 0.003$), and hyperlipidemia (32.3% vs. 0%; $P = 0.002$). Finally, hospitalization was more frequent in resistant patients (81.2% vs. 22.7%; $P < 0.001$).

Conclusion: These findings indicate that aspirin resistance is prevalent among Iranian CAD patients and is strongly associated with older age and increased cardiovascular risk factors, underscoring its clinical significance. Routine screening for aspirin resistance should be integrated into CAD management protocols, enabling personalized antiplatelet strategies and ultimately improving patient outcomes.

Keywords: Coronary artery disease, Aspirin resistance, BT, Chest pain, Cardiovascular risk factors

Introduction

Coronary artery disease (CAD) is a chronic cardiovascular condition marked by the gradual narrowing or blockage of the coronary arteries, usually caused by atherosclerosis, which decreases blood flow to the myocardium over time (1, 2). CAD is a major public health challenge and a leading cause of morbidity and mortality in industrialized nations, including the United States, where prevalence reached 4.9% among adults in 2022 (2-4). In developing countries like Iran, cardiovascular diseases account for 36% of all deaths, with myocardial infarction (MI) as the main cause (5, 6).

Long-term use of antiplatelet drugs can reduce the

annual risk of major vascular events, such as non-fatal heart attacks, strokes, or vascular deaths, by about 25% (7). They also help prevent thrombotic events. Among antiplatelet drugs, aspirin is the most studied and is recommended at a minimum daily dose of 75 mg (8, 9). Its principal role is the irreversible inhibition of platelet cyclooxygenase-1 (COX-1), which inhibits the conversion of arachidonic acid to thromboxane A₂, consequently preventing platelet aggregation and thrombus formation (10-12).

Aspirin resistance describes the inability of aspirin to inhibit COX-1 activity, leading to ongoing platelet thromboxane A₂ production and aggregation despite



therapeutic doses (13). Reports of varying patient responses to aspirin have emerged over the past decades, with prevalence rates differing across regions due to biological and genetic heterogeneity (13-16).

Clinically, individuals with laboratory-confirmed aspirin resistance (high on-treatment platelet reactivity) with stable cardiovascular disease have a more than twofold increased risk of major adverse cardiovascular events compared with aspirin-sensitive patients (17). Strategies like increasing aspirin dosage or combining it with other antiplatelet agents often fail to overcome resistance, highlighting the difficulty of optimizing treatment in this group (18).

Although developed countries have extensively studied aspirin resistance, data from Iran, especially among CAD patients presenting to emergency departments, are still limited. Significant gaps remain in our understanding of the precise molecular mechanisms, standardized detection methods, and effective management strategies for aspirin resistance. This study, therefore, aims to assess the prevalence and clinical implications of aspirin resistance in Iranian patients with chest pain on aspirin therapy, accounting for population differences and potential genetic factors.

Materials and Methods

This prospective cross-sectional study was conducted at the Emergency Department of Imam Hussein Hospital, Tehran, Iran, from April to December 2021. A total of 155 patients with angiographically confirmed CAD on daily aspirin therapy were enrolled consecutively using convenience sampling. Bleeding time was measured by the SimPlate method. Data were analyzed using SPSS v21. Normality was assessed by the Shapiro-Wilk test, and group comparisons were conducted via independent-samples *t*-tests for continuous variables and χ^2 tests for categorical variables; $P < 0.05$ was considered statistically significant. The protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1394.127).

Inclusion criteria included

1. Individuals diagnosed with CAD via angiography and referred for typical chest pain.
2. Patients aged 18 years or older.
3. Daily aspirin therapy (≥ 75 mg) for at least 7 days prior to presentation.

Exclusion criteria included

1. Concurrent use of anticoagulants (rivaroxaban, enoxaparin, or warfarin).
2. Use of NSAIDs within the past two weeks.
3. History of bleeding disorders or platelet count $< 150,000/\text{mm}^3$.
4. Hemoglobin < 8 g/dL.
5. Severe hepatic or renal dysfunction.
6. Active malignancy.
7. Discontinuation of aspirin on the day of enrollment.

The minimum sample size was calculated using the following formula

$$N = \frac{Z^2 \times P(1-P)}{d^2}$$

where $Z = 1.96$ (95% confidence level) and $P = 0.75$. The prevalence (P) was estimated based on a previous study of the Iranian population (19) and a d of 0.07, yielding $N = 155$ patients. The margin of error ($d = 0.07$) was selected to balance the desired accuracy with the practical constraints of the study duration and the strict exclusion criteria used in patient selection, ensuring feasible data collection within available resources.

Demographic data, clinical laboratory tests, imaging, and procedures, including ECG, echocardiography, and coronary angiography findings, were documented. Risk factors for coronary artery disease, including hypertension, diabetes, hyperlipidemia, and smoking, were also documented. The bleeding time (BT) recorded by the SimPlate method involves inflating a blood pressure cuff to 40–45 mmHg on the forearm, making a 3 mm incision, and blotting blood with filter paper every 30 seconds without touching the wound. The duration until bleeding stops is recorded in seconds. After reviewing troponin and ECG results twice (6 hours apart), the patients were evaluated in the emergency room until the decision was made whether to hospitalize or discharge them. Finally, patient outcomes were recorded.

Descriptive statistics, including mean, median, standard deviation, and frequencies, were used. The normality of continuous variables was evaluated with the Shapiro-Wilk test, and normally distributed data were compared using the independent-samples *t*-test. The chi-square test was employed to compare categorical variables. Demographic data were visualized using charts. P -values less than 0.05 were considered statistically significant. The analysis was performed using SPSS version 21.

Results

This study enrolled 155 patients treated with aspirin, including 92 (59.4%) men, with an average age of 57.49 ± 13.13 years. Of these, 53 patients (34.2%) were aged 61–70. High blood pressure was the most common risk factor, affecting 60 cases (38.7%). Additionally, 55 patients (35.5%) had two cardiovascular risk factors, 28 (18.1%) had a history of angiography, and 7 (4.5%) had stents implanted. Laboratory data are recorded in [Table 1](#). ([Figures 1 and 2](#))

We adopted the $\text{BT} < 5$ minutes cutoff based on the standardization of the SimPlate method and previous research establishing this threshold for insufficient platelet inhibition by aspirin (20, 21). The average BT was 3.48 ± 0.99 minutes. Aspirin resistance ($\text{BT} < 5$) was observed in 133 (85.8%) patients. [Table 2](#) shows the association between aspirin resistance and patient age.

Ultimately, 42 patients (27.1%) were discharged without hospitalization. Analysis showed that older patients had more aspirin resistance than those with adequate aspirin

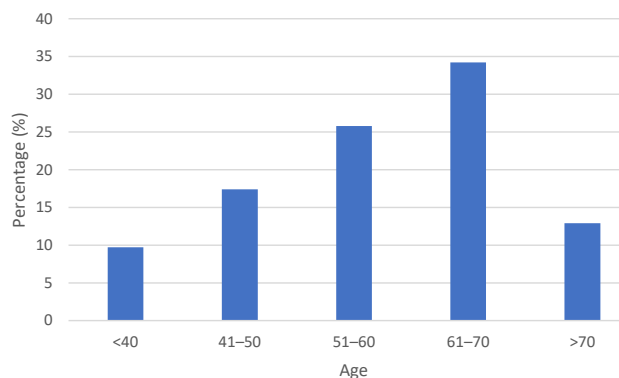


Figure 1. Distribution of coronary artery disease patients across age groups



Figure 2. Relative frequency of key cardiovascular risk factors among the study population

Table 1. Laboratory test results of studied patients (N=155). Data are presented as mean±standard deviation; descriptive statistics only (no inferential tests applied). Abbreviations: WBC, white blood cell count; SD: standard deviation; PTT: partial thromboplastin time; INR: international normalized ratio

Variable (unit)	Mean (±SD)
WBC ($\times 10^3/\text{mm}^3$)	8.54±2.74
Hemoglobin (g/dL)	12.95±3.50
Hematocrit (%)	37.88±12.30
Platelets ($\times 10^3/\text{mm}^3$)	214.00±145.00
Urea (mg/dL)	37.62±14.50
Creatinine (mg/dL)	1.26±0.60
PTT (seconds)	22.00±9.00
INR (unitless)	1.20±0.20

function ($P<0.001$). The gender of patients with aspirin resistance was also recorded. The results indicated no significant association between patient gender and aspirin resistance ($P=0.363$).

Patients with appropriate aspirin use had significantly fewer cardiovascular disease risk factors than those without ($P<0.001$)(Figure 3).

When examining cardiovascular risk factors associated with aspirin resistance, the rates of hypertension and diabetes were significantly higher in aspirin-resistant patients than in the other groups.

Table 3 Association between aspirin resistance and patient risk factors

Analysis of discharge status showed that 108 patients (81.2%) who were aspirin-resistant required hospitalization compared to only 5 (22.7%) aspirin-sensitive patients. Conversely, 25 (18.8%) aspirin-resistant patients and 17 (77.3%) aspirin-sensitive patients were discharged from the emergency department. This difference was statistically significant ($P<0.001$).

Discussion

This study enrolled 155 patients undergoing daily aspirin therapy. The results revealed a markedly high prevalence of aspirin resistance (85.8%) among Iranian patients with CAD presenting to the emergency department. The main findings are as follows: 1) a high prevalence of aspirin resistance within the studied Iranian cohort, 2) significant associations between aspirin resistance

and conditions such as hypertension, diabetes mellitus, and hyperlipidemia, 3) a notably higher occurrence of aspirin resistance among older patients, 4) poorer clinical outcomes in aspirin-resistant patients, who also required more frequent hospitalization, and 5) significant contribution of methodological factors to variability in the prevalence of aspirin resistance.

However, the remarkably high prevalence observed in our study significantly exceeds the typical international range of 5% to 60% (22, 23), but closely aligns with previous regional reports by Zimmermann et al., Ziaie et al., and Sadeghi et al. (19, 24, 25), indicating that aspirin resistance prevalence may vary significantly based on population-specific environmental and genetic factors. Genetic polymorphisms, particularly in cyclooxygenase pathways (COX-1 and COX-2), substantially influence aspirin response (26). Variants such as rs3842787 (COX-1) and rs20417 (COX-2) have been strongly associated with reduced platelet responsiveness and elevated cardiovascular risks (27). Population-specific genetic studies further underscore the influence of ethnic variations on pharmacodynamic responses to aspirin, highlighting the need for targeted screening and therapeutic interventions in genetically predisposed populations.

Our finding of significant associations between aspirin resistance and cardiovascular risk factors, including hypertension, diabetes mellitus, and hyperlipidemia, supports previous studies (28, 29). Diabetes mellitus enhances platelet reactivity via several mechanisms, including oxidative stress, glycation of platelet surface proteins, and dysregulated platelet signaling pathways, all of which diminish aspirin efficacy (30, 31). DiChiara et al. specifically demonstrated higher aspirin resistance rates among diabetic patients, emphasizing the clinical necessity for alternative or adjunctive antiplatelet strategies in these individuals (32). Hypertension similarly influences platelet function, likely through shear-stress-induced platelet activation, suggesting that careful blood pressure management might mitigate aspirin resistance in hypertensive patients (33).

We observed a significant correlation between older age and increased aspirin resistance, consistent with existing literature. Aging is associated with physiological

Table 2. Comparison of gender distribution and mean age between aspirin-resistant and aspirin-sensitive patients ($N=155$). Categorical data are presented as n (%); continuous data as mean \pm SD. Gender distribution was compared using Pearson's chi-square test, and age differences were assessed by an independent-samples t -test. χ^2 test for gender ($\alpha=0.05$); independent-samples t -test for age ($\alpha=0.05$); Significance Level: $\alpha=0.05$; SD: standard deviation; n : number of patients.

Group	N	Gender		Age Mean (\pm SD)	P-value
		Male (%)	Female (%)		
Aspirin-resistant	133	77 (57.9)	56 (42.1)	59.64 \pm 12.47	<0.001
Aspirin-sensitive	22	15 (68.2)	7 (31.8)	44.50 \pm 9.05	–

Table 3. Association between aspirin resistance and patient risk factors. Data are presented as n (%). Comparisons between aspirin-resistant and aspirin-sensitive groups were performed using Pearson's chi-square test for all risk factors; Fisher's exact test was used where any expected cell count was <5 (e.g., alcohol consumption). Significance level: $\alpha=0.05$; n : number

Risk Factor	Aspirin-resistant		Aspirin-sensitive		P-value
	Present	Absent	Present	Absent	
Hypertension	56 (42.1)	77 (57.9)	4 (18.2)	18 (81.8)	0.033
Diabetes mellitus	57 (42.9)	76 (57.1)	2 (9.1)	20 (90.9)	0.003
Smoking	25 (18.8)	108 (81.2)	5 (22.7)	17 (77.3)	0.666
Ischemic heart Disease	17 (12.8)	116 (87.2)	1 (4.5)	21 (95.5)	0.264
Alcohol Consumption	4 (3.0)	129 (97.0)	0 (0.0)	22 (100.0)	0.410
Hyperlipidemia	43 (32.3)	90 (67.7)	0 (0.0)	22 (100.0)	0.002

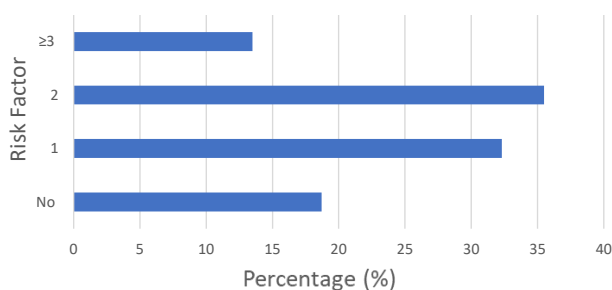


Figure 3. Histogram of the number of concurrent risk factors per patient

changes, including altered drug metabolism, decreased renal function, increased platelet aggregation, and chronic low-grade inflammation, all of which contribute to reduced responsiveness to antiplatelet medications (34, 35). Targeted dosing strategies, higher-dose aspirin therapy, or combining aspirin with alternative antiplatelet agents (such as clopidogrel or ticagrelor) could potentially improve clinical outcomes in older aspirin-resistant patients, as suggested by several recent studies (36, 37).

Clinically, aspirin-resistant patients demonstrated poorer outcomes, primarily reflected in increased hospitalization rates. This reinforces previous observations by Chen et al. (15) and Chen et al. (38), underscoring the need for routine, accurate detection of aspirin resistance to improve clinical decision-making and patient outcomes. While BT offers practical benefits in emergency settings, more specific methods, such as the platelet function analyzer-100 (PFA-100) and light transmission aggregometry (LTA), could provide greater diagnostic accuracy and should be considered when feasible (39, 40).

Considering the link between aspirin resistance in CAD patients and various cardiovascular risk factors, there is an increased risk of cardiovascular complications and events, such as angina pectoris, as well as higher mortality, in those with aspirin resistance compared with those without (41, 42). Thus, regular screening with reasonable

tools may be essential to identify these patients.

Limitations

This study faced several limitations, including the use of a single, less specific method (BT) for assessing aspirin resistance, a cross-sectional design that limits causal inference, and convenience sampling. Although convenience sampling is practical and efficient, it may restrict causal inference and introduce bias in patient selection, potentially limiting the generalizability of the findings. To strengthen evidence in future research, employing prospective longitudinal designs, randomized controlled trials, and more precise laboratory assessments of platelet function, such as the Platelet Function Analyzer-100 (PFA-100), light transmission aggregometry (LTA), and biochemical assays (e.g., thromboxane B2 levels), will be beneficial.

Finally, while univariate analyses demonstrated significant associations between aspirin resistance and risk factors (such as diabetes and age), a multivariate analysis to adjust for potential confounders was not performed in this study. Therefore, the reported associations should be interpreted with caution, as the independent effect of each variable remains to be fully established in future studies with larger sample sizes.

Conclusion

Given the high prevalence of aspirin resistance in the Iranian population, routine screening is needed, especially for older patients and those with cardiovascular risk factors. Aspirin resistance testing should be standard for CAD patients who need it. Early identification of resistant patients can guide personalized antiplatelet therapy to improve clinical outcomes.

Authors' Contribution

Conceptualization: Anita Sabzghabaei

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Competing Interests

None to be declared.

Ethical Approval

The study adhered to the principles of the Declaration of Helsinki and was conducted with approval from the Ethics Committee of Shahid Beheshti University of Medical Sciences (approval No. IR.SBMU.MSP.REC.1394.127). All patients provided informed consent before their inclusion.

Funding

This study was self-funded by the authors.

References

- Pintea Bentea G, Berdaoui B, Morissens M, van de Borne P, Castro Rodriguez J. Pathophysiology, diagnosis, and management of coronary artery disease in the setting of atrial fibrillation. *J Am Heart Assoc* 2024;13(23):e037552. doi:10.1161/jaha.124.037552
- Mack M, Gopal A. Epidemiology, traditional and novel risk factors in coronary artery disease. *Heart Fail Clin* 2016;12(1):1-10. doi:10.1016/j.hfc.2015.08.002
- Dai H, Much AA, Maor E, Asher E, Younis A, Xu Y, et al. Global, regional, and national burden of ischaemic heart disease and its attributable risk factors, 1990-2017: results from the Global Burden of Disease Study 2017. *Eur Heart J Qual Care Clin Outcomes* 2022;8(1):50-60. doi:10.1093/ehjqcco/qcaa076
- Khalid N, Haider S, Abdullah M, Asghar S, Laghari MA, Rajeswaran Y. Trends and disparities in coronary artery disease prevalence among US adults from 2019 to 2022. *Curr Probl Cardiol* 2024;49(8):102645. doi:10.1016/j.cpcardiol.2024.102645
- Gerber Y, Weston SA, Jiang R, Roger VL. The changing epidemiology of myocardial infarction in Olmsted county, Minnesota, 1995-2012. *Am J Med* 2015;128(2):144-51. doi:10.1016/j.amjmed.2014.09.012
- Loscalzo J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. Harrison's Principles of Internal Medicine. 21st ed. McGraw Hill; 2022.
- Gelbenegger G, Postula M, Pecan L, Halvorsen S, Lesiak M, Schoergenhofer C, et al. Aspirin for primary prevention of cardiovascular disease: a meta-analysis with a particular focus on subgroups. *BMC Med* 2019;17(1):198. doi:10.1186/s12916-019-1428-0
- Gu Q, Dillon CF, Eberhardt MS, Wright JD, Burt VL. Preventive aspirin and other antiplatelet medication use among US adults aged ≥40 years: data from the National Health and Nutrition Examination Survey, 2011-2012. *Public Health Rep* 2015;130(6):643-54. doi:10.1177/003335491513000614
- Van't Hof JR, Duval S, Oldenburg NC, Misialek JR, Eder MM, Jones C, et al. Low-dose aspirin for primary prevention of cardiovascular disease: trends in use patterns among African American adults in Minnesota, 2015-2019. *Prev Med* 2021;148:106589. doi:10.1016/j.ypmed.2021.106589
- Protty MB, Tyrrell VJ, Hajeyah AA, Morgan B, Costa D, Li Y, et al. Aspirin modulates generation of procoagulant phospholipids in cardiovascular disease, by regulating LPCAT3. *J Lipid Res* 2025;66(1):100727. doi:10.1016/j.jlr.2024.100727
- Ahn TG, Hwang JY. Preeclampsia and aspirin. *Obstet Gynecol Sci* 2023;66(3):120-32. doi:10.5468/ogs.22261
- Giménez-Bastida JA, Boeglin WE, Boutaud O, Malkowski MG, Schneider C. Residual cyclooxygenase activity of aspirin-acetylated COX-2 forms 15 R-prostaglandins that inhibit platelet aggregation. *FASEB J* 2019;33(1):1033-41. doi:10.1096/fj.201801018R
- Khan H, Kanny O, Syed MH, Qadura M. Aspirin resistance in vascular disease: a review highlighting the critical need for improved point-of-care testing and personalized therapy. *Int J Mol Sci* 2022;23(19):11317. doi:10.3390/ijms231911317
- Du G, Lin Q, Wang J. A brief review on the mechanisms of aspirin resistance. *Int J Cardiol* 2016;220:21-6. doi:10.1016/j.ijcard.2016.06.104
- Chen HY, Chou P. PFA-100-measured aspirin resistance is the predominant risk factor for hospitalized cardiovascular events in aspirin-treated patients: a 5-year cohort study. *J Clin Pharm Ther* 2018;43(2):249-55. doi:10.1111/jcpt.12643
- Ebrahimi P, Farhadi Z, Behzadifar M, Shabaninejad H, Abolghasem Gorji H, Taheri Mirghaed M, et al. Prevalence rate of laboratory defined aspirin resistance in cardiovascular disease patients: a systematic review and meta-analysis. *Caspian J Intern Med* 2020;11(2):124-34. doi:10.22088/cjim.11.2.124
- Han YL. Aspirin resistance in coronary heart disease: current understandings and strategies. *J Transl Int Med* 2016;4(1):7-10. doi:10.1515/jtim-2016-0002
- Arockiam S, Staniforth B, Kepreotis S, Maznyczka A, Bulluck H. A contemporary review of antiplatelet therapies in current clinical practice. *Int J Mol Sci* 2023;24(13):11132. doi:10.3390/ijms241311132
- Sadeghi M, Emami A, Ziyaei N, Yaran M, Golabchi A, Sadeghi A. Aspirin resistance and ischemic heart disease on Iranian experience. *Adv Biomed Res* 2012;1:33. doi:10.4103/2277-9175.99345
- Sundram E, Kharaharilal P, Ilavarasu S, Renukadevi, Nalini E, Karunamoorthy V. Evaluative comparison of systemic aspirin therapy effects on gingival bleeding in post non-surgical periodontal therapy individuals. *J Pharm Bioallied Sci* 2012;4(Suppl 2):S221-5. doi:10.4103/0975-7406.100210
- Russeau AP, Vall H, Manna B. Bleeding time. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2023.
- Yassin AS, Abubakar H, Mishra T, Subahi A, Hartman M, Ahmed A, et al. Aspirin resistance: cardiovascular risk game changer. *Am J Ther* 2019;26(5):593-9. doi:10.1097/mjt.0000000000000780
- Cai G, Zhou W, Lu Y, Chen P, Lu Z, Fu Y. Aspirin resistance and other aspirin-related concerns. *Neurol Sci* 2016;37(2):181-9. doi:10.1007/s10072-015-2412-x
- Ziaie N, Sadeghi M, Akhlaghi A, Pirhaji O, Yaran M, Pourmoghadam M. Aspirin resistance status as determined by urinary thromboxane B2 (TXB2) level in patients with ischemic heart disease and its relationship with severity of coronary artery disease. *J Isfahan Med Sch* 2010;28(116):1008-15.
- Zimmermann N, Hohlfeld T. Clinical implications of aspirin resistance. *Thromb Haemost* 2008;100(3):379-90. doi:10.1160/TH08-01-0056
- Li CX, Sun LC, Wang YQ, Liu TT, Cai JR, Liu H, et al. The associations of candidate gene polymorphisms with aspirin resistance in patients with ischemic disease: a meta-analysis. *Hum Genomics* 2024;18(1):135. doi:10.1186/s40246-024-00699-1

27. Yi X, Cheng W, Lin J, Zhou Q, Wang C. Interaction between COX-1 and COX-2 variants associated with aspirin resistance in Chinese stroke patients. *J Stroke Cerebrovasc Dis* 2016;25(9):2136-44. doi:10.1016/j.jstrokecerebrovasdis.2016.05.039
28. Bobescu E, Covaciu A, Rus H, Radoi M, Badea M, Moga SN, et al. Correlation of cardiovascular risk factors and biomarkers with platelet reactivity in coronary artery disease. *Am J Ther* 2019;26(5):563-9. doi:10.1097/mjt.0000000000000869
29. Li Y, Xie Y, Wang L, Zhang Y, Gu H, Chai Y. Significant modules and biological processes between active components of *Salvia miltiorrhiza* deposite salt and aspirin. *Evid Based Complement Alternat Med* 2016;2016:3439521. doi:10.1155/2016/3439521
30. Rivas Rios JR, Franchi F, Rollini F, Angiolillo DJ. Diabetes and antiplatelet therapy: from bench to bedside. *Cardiovasc Diagn Ther* 2018;8(5):594-609. doi:10.21037/cdt.2018.05.09
31. Santilli F, Lapenna D, La Barba S, Davi G. Oxidative stress-related mechanisms affecting response to aspirin in diabetes mellitus. *Free Radic Biol Med* 2015;80:101-10. doi:10.1016/j.freeradbiomed.2014.12.010
32. DiChiara J, Bliden KP, Tantry US, Hamed MS, Antonino MJ, Suarez TA, et al. The effect of aspirin dosing on platelet function in diabetic and nondiabetic patients: an analysis from the aspirin-induced platelet effect (ASPECT) study. *Diabetes* 2007;56(12):3014-9. doi:10.2337/db07-0707
33. Blann AD, Nadar S, Lip GY. Pharmacological modulation of platelet function in hypertension. *Hypertension* 2003;42(1):1-7. doi:10.1161/01.Hyp.0000077901.84467.E1
34. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol* 2004;57(1):6-14. doi:10.1046/j.1365-2125.2003.02007.x
35. Le Blanc J, Lordkipanidzé M. Platelet function in aging. *Front Cardiovasc Med* 2019;6:109. doi:10.3389/fcvm.2019.00109
36. Yi X, Lin J, Wang C, Huang R, Han Z, Li J. Platelet function-guided modification in antiplatelet therapy after acute ischemic stroke is associated with clinical outcomes in patients with aspirin nonresponse. *Oncotarget* 2017;8(63):106258-69. doi:10.18632/oncotarget.22293
37. Khan H, Gallant R, Jain S, Al-Omran M, De Mestral C, Greco E, et al. Ticagrelor as an alternative antiplatelet therapy in cardiac patients non-sensitive to aspirin. *Medicina (Kaunas)* 2020;56(10):519. doi:10.3390/medicina56100519
38. Chen WH, Cheng X, Lee PY, Ng W, Kwok JY, Tse HF, et al. Aspirin resistance and adverse clinical events in patients with coronary artery disease. *Am J Med* 2007;120(7):631-5. doi:10.1016/j.amjmed.2006.10.021
39. Posan E, McBane RD, Grill DE, Motsko CL, Nichols WL. Comparison of PFA-100 testing and bleeding time for detecting platelet hypofunction and von Willebrand disease in clinical practice. *Thromb Haemost* 2003;90(3):483-90. doi:10.1160/th03-02-0111
40. Hayward CP, Moffat KA, Raby A, Israels S, Plumhoff E, Flynn G, et al. Development of North American consensus guidelines for medical laboratories that perform and interpret platelet function testing using light transmission aggregometry. *Am J Clin Pathol* 2010;134(6):955-63. doi:10.1309/ajcp9v3rrvnmkds
41. Shao C, Wang J, Tian J, Tang YD. Coronary artery disease: from mechanism to clinical practice. *Adv Exp Med Biol* 2020;1177:1-36. doi:10.1007/978-981-15-2517-9_1
42. Paven E, Dillinger JG, Bal Dit Sollier C, Vidal-Trecan T, Berge N, Dautry R, et al. Determinants of aspirin resistance in patients with type 2 diabetes. *Diabetes Metab* 2020;46(5):370-6. doi:10.1016/j.diabet.2019.11.002