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Review Article

ASPIRIN HYPERSENSITIVITY IN CORONARY ARTERY DISEASE: PRACTICAL CHALLENGES AND MANAGEMENT APPROACHES

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ABSTRACT: Aspirin is a cornerstone therapy for coronary artery disease (CAD), yet hypersensitivity complicates its use in clinical practice. This narrative review synthesizes contemporary evidence from studies and guidelines to provide pragmatic, evidence–based recommendations on the epidemiology, mechanisms, classification, and management of aspirin hypersensitivity. Prevalence is estimated at 0.5–1.9% in the general population and 2.6% among patients undergoing coronary angiography. In the ADAPTED (Aspirin Desensitization in Patients with Coronary Artery Disease) registry, a rapid desensitization protocol achieved a 95.4% success rate, with 80.3% of patients remaining on aspirin at 12 months. The 2025 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend aspirin desensitization as the preferred strategy in acute coronary syndromes (ACS). In contrast, the 2024 European Society of Cardiology (ESC) guidelines recommend clopidogrel for chronic coronary syndromes (CCS) when aspirin is not tolerated. Desensitization is contraindicated in patients with a history of severe anaphylaxis. Accordingly, desensitization should be preferred whenever feasible. When it is not possible or unsuccessful, alternatives—such as cilostazol, indobufen, or P2Y12 inhibitor–based regimens with or without oral anticoagulants—may be considered based on ischemic and bleeding risk. Robust randomized controlled trials are needed to confirm the efficacy of these strategies.

Keywords: aspirin hypersensitivity, aspirin desensitization, coronary artery disease

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1. INTRODUCTION

Aspirin remains a cornerstone antiplatelet agent in the management of coronary artery disease (CAD), with established benefits in both acute and chronic clinical settings. The 2025 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend the administration of an initial loading dose of aspirin followed by long-term low-dose maintenance therapy in patients with acute coronary syndromes (ACS) to reduce mortality and major adverse cardiovascular events (MACE) (Class of Recommendation [COR] I, Level of Evidence [LOE] A) [1]. Likewise, the 2024 European Society of Cardiology (ESC) guidelines endorse lifelong aspirin therapy at a daily dose of 75–100 mg for patients with chronic coronary syndromes (CCS) and a history of myocardial infarction (MI), percutaneous coronary intervention (PCI), or coronary artery bypass grafting (Class I, LOE A). Compared with no treatment, aspirin confers a substantial reduction in cardiovascular mortality and major vascular events, including nonfatal MI and nonfatal stroke [2].

Despite its well-established role, a small subset of patients experience aspirin hypersensitivity, particularly in the setting of ACS where timely PCI is required, thereby posing significant therapeutic challenges. The reported prevalence of aspirin hypersensitivity is approximately 0.5–1.9% in the general population and up to 2.6% among patients undergoing coronary angiography [3,4].

Management of CAD in patients with aspirin hypersensitivity or intolerance remains difficult, as these populations are underrepresented in randomized clinical trials (RCTs). Notably, in Vietnam, there are currently no specific recommendations regarding the management of aspirin hypersensitivity in CAD.

The present review aims to provide an updated synthesis of the epidemiology, pathophysiological mechanisms, clinical classification, and management strategies of aspirin hypersensitivity in CAD, with a particular focus on practical implications for clinical practice.

2. EPIDEMIOLOGY

Although relatively uncommon in the general population, aspirin hypersensitivity represents a substantial challenge in interventional cardiology, as aspirin remains the cornerstone of antiplatelet therapy. Globally, the prevalence of aspirin hypersensitivity has been reported at approximately 0.5–1.9% in the general population, rising to as high as 25% among patients with asthma or nasal polyps, and 27–35% among those with chronic urticaria [3]. The prevalence of aspirin hypersensitivity among patients with MI has not been clearly established. Within cardiovascular cohorts, about 1.5% of patients report a history of adverse reactions to aspirin; however, only 21% of these cases fulfill diagnostic criteria for true hypersensitivity. Another study demonstrated that 2.6% of patients admitted for coronary angiography reported a history of aspirin hypersensitivity [4].

In the Asia-Pacific region, the prevalence of nonsteroidal anti-inflammatory drug (NSAID) hypersensitivity in adults appears relatively low. In cohorts of patients with chronic rhinosinusitis in China, based on medical history, the prevalence was reported between 0.28% and 1.46%. A separate retrospective analysis identified 346 cases of NSAID hypersensitivity reported over a 30–year period (1979–2010) in the China Academic Journal Network Publishing Database. In South Korea, the COREA (COhort for Reality and Evolution of Adult Asthma) study documented aspirin–intolerant asthma in 5.8% (68/1,173) of adult asthmatics [3]. To date, no systematic investigations have been conducted in Vietnam. In clinical practice, most reports of aspirin hypersensitivity are based on patient history, given the absence of standardized diagnostic tools.

3. PATHOPHYSIOLOGY OF ASPIRIN HYPERSENSITIVITY

Aspirin, a salicylic acid–derived NSAID, exerts its effects through the irreversible inhibition of the cyclooxygenase (COX) activity of prostaglandin H synthase isoenzymes 1 and 2 (COX-1 and COX-2). This inhibition suppresses the production of thromboxane

A_2 (TXA_2) and prostacyclin (PGI_2). At low doses, aspirin selectively inhibits COX-1, while higher doses inhibit both COX-1 and COX-2. Through inhibition of the TXA_2 pathway, aspirin attenuates platelet activation and aggregation—two critical steps in the pathogenesis of thrombosis and MI. Furthermore, the inhibition of platelet activation at sites of vascular injury results in indirect effects beyond TXA_2 suppression, including reduced release of inflammatory cytokines, reactive oxygen species, and growth factors. In contrast to TXA_2, PGI_2 plays a vasoprotective role by counteracting atherosclerosis and thrombosis. Since low-dose aspirin minimally affects COX-2– and PGI_2-mediated vascular function, it does not cause hypertension, renal impairment, or reduce the efficacy of diuretics or angiotensin-converting enzyme inhibitors [5].

NSAID hypersensitivity was first classified by Stevenson et al. based on clinical presentation, underlying disease, and cross-reactivity with other COX-1 inhibitors. In 2013, the European Academy of Allergy and Clinical Immunology/European Network for Drug Allergy (EAACI/ENDA) distinguished two principal mechanisms of NSAID hypersensitivity: cross-reactive (non-immunologic mediated) and selective (immunologically mediated) reactions [6].

Most patients with NSAID hypersensitivity develop symptoms upon exposure to two or more chemically unrelated NSAIDs that share COX-1 inhibition. This phenotype, termed "cross-reactive" hypersensitivity, is driven by non-immunologic mediated mechanisms. COX-1 inhibition reduces prostaglandin E_2 (PGE_2) synthesis and diverts arachidonic acid (AA) metabolism toward the cysteinyl leukotriene (CysLTs: LTC_4, LTD_4, LTE_4) pathway, which exerts pro-inflammatory effects and triggers hypersensitivity reactions in susceptible individuals. In this process, AA is oxidized in inflammatory leukocytes by the 5-lipoxygenase (5-LO) enzyme to form leukotriene A_4 (LTA_4) [Figure 1]. Clinical factors such as asthma, chronic rhinosinusitis, nasal polyps, female sex, and chronic urticaria further increase the risk of hypersensitivity to aspirin and other NSAIDs [6,7].

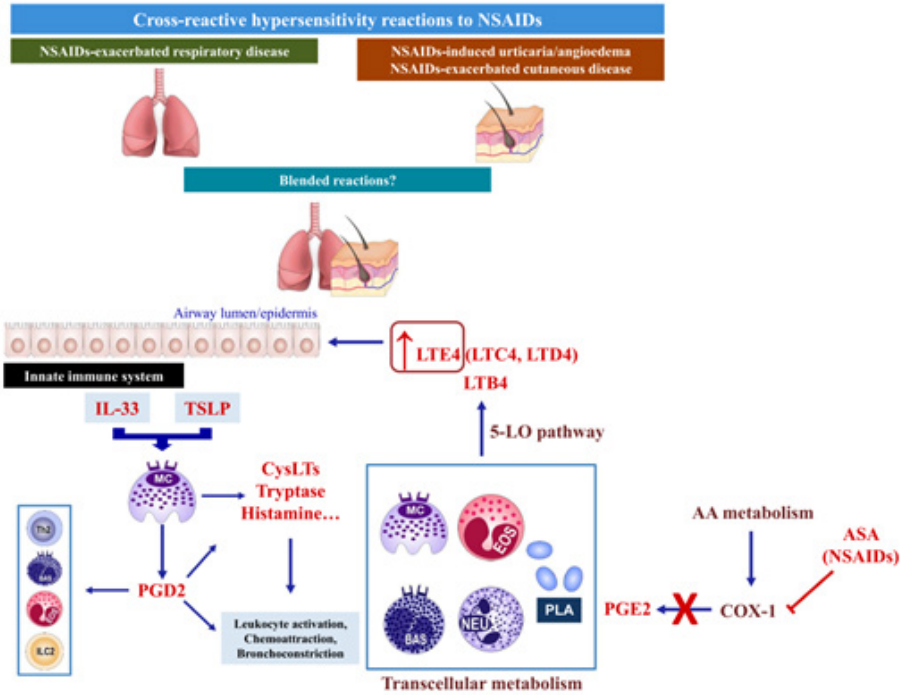

Figure 1. Cross-reactive hypersensitivity reactions to NSAIDs. Reprinted from [6], with permission from John Wiley & Sons Ltd. © 2019 EAACI and John Wiley & Sons A/S.

In some patients, hypersensitivity symptoms occur only after exposure to a single NSAID (or to multiple agents within the same chemical class), while other chemically unrelated NSAIDs are generally well tolerated. These reactions are considered immunologically mediated and are referred to as selective hypersensitivity. Single-NSAID hypersensitivity

may be mediated by either immunoglobulin E (IgE) or T cells. In the immediate, IgE-mediated mechanism, NSAIDs—being low-molecular-weight compounds—must bind to carrier proteins to form hapten-protein complexes. Following sensitization, these complexes are presented by antigen-presenting cells to Th2 lymphocytes, which stimulate B cells to produce drug-specific IgE. The IgE binds to the surface of mast cells and basophils. Upon re-exposure, the drug cross-links adjacent IgE molecules, triggering cellular degranulation and the release of histamine, tryptase, chymase, prostaglandin D_2 (PGD_2) and CysLTs, leading to urticaria, angioedema, or anaphylaxis. In the delayed, T-cell–mediated mechanism, drug-protein complexes are presented via HLA class I molecules to CD8+ T cells or via HLA class II molecules to CD4+ T cells. CD4+ T cells differentiate into Th1 cells and secrete interferon-γ (IFN-γ), driving inflammation, while CD8+ T cells become cytotoxic lymphocytes releasing perforin and granzyme B, leading to cell lysis. Upon re-exposure, this pathway results in delayed inflammatory reactions and tissue injury [Figure 2] [6,7].

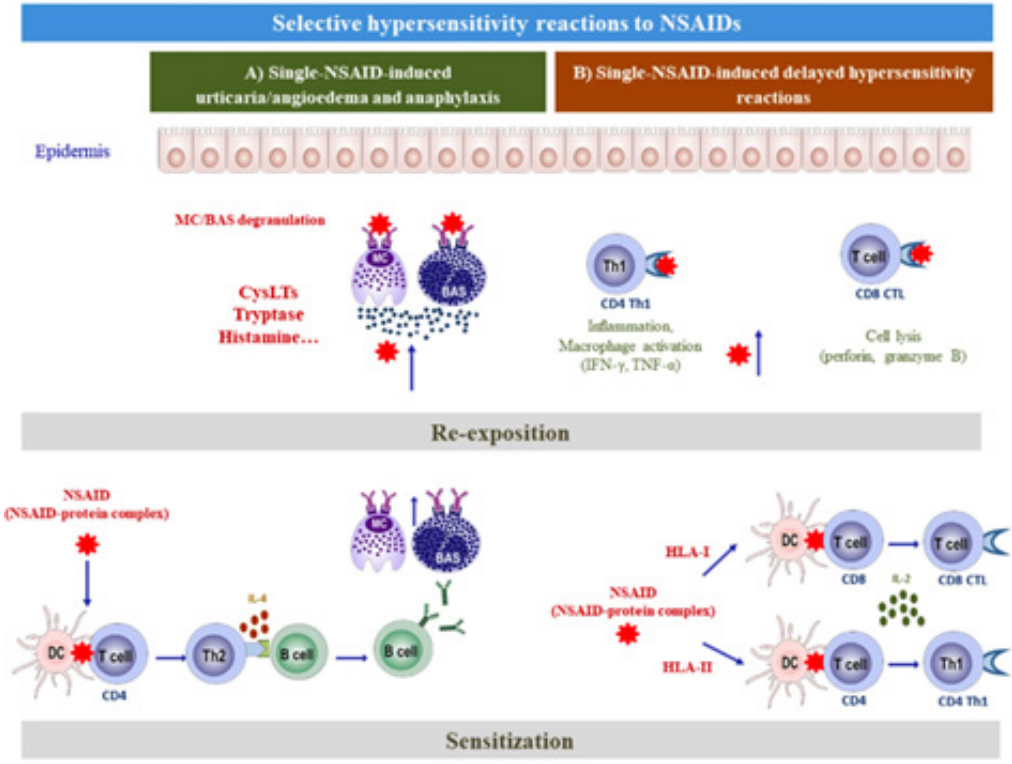

Figure 2. Selective hypersensitivity reactions to NSAIDs. Reprinted from [6], with permission from John Wiley & Sons Ltd. © 2019 EAACI and John Wiley & Sons A/S.

Beyond the spectrum of culprit drugs, the timing of symptom onset (immediate versus delayed) may also reflect the underlying mechanism, whether immunologically mediated (IgE- or T-cell–driven) or non-immunologic mediated (cross-reactive). It is important to note that, in clinical practice, blended reactions not fully aligned with existing classification systems may occur [7].

Understanding these mechanisms not only clarifies the respiratory or cutaneous manifestations of hypersensitivity but also provides the basis for implementing aspirin desensitization protocols or selecting appropriate therapeutic alternatives in CAD.

4. CLASSIFICATION OF ASPIRIN HYPERSENSITIVITY

The EAACI/ENDA classifies hypersensitivity reactions to aspirin—and NSAIDs more broadly—into two major categories: immunologically mediated and non-immunologic mediated [Table 1] [7].

Non-immunologic mediated (cross-reactive) hypersensitivity reactions to NSAIDs

NSAIDs-exacerbated respiratory disease (NERD): Hypersensitivity reactions induced by aspirin or other NSAIDs, presenting primarily with bronchospasm, dyspnea, nasal congestion, and/or rhinorrhea, typically in patients with underlying chronic respiratory conditions such as asthma, chronic rhinosinusitis, or nasal polyps. Historical terms include aspirin triad, asthma triad, Samter's syndrome, Widal syndrome, aspirin-induced asthma, aspirin-sensitive rhinosinusitis/asthma syndrome, aspirin-intolerant asthma and aspirin-exacerbated respiratory disease.

NSAIDs-exacerbated cutaneous disease (NECD): Hypersensitivity reactions to aspirin or other NSAIDs manifesting as wheals and/or angioedema in patients with a history of chronic spontaneous urticaria. Previous terms include aspirin-induced urticaria and aspirin-exacerbated cutaneous disease.

NSAIDs-induced urticaria/angioedema (NIUA): Hypersensitivity reactions caused by aspirin or other NSAIDs, manifesting as wheals and/or angioedema in otherwise healthy individuals without a history of chronic spontaneous urticaria. Symptoms occur following exposure to at least two chemically unrelated NSAIDs (belonging to different structural classes).

Immunologically mediated (non-cross-reactive) hypersensitivity reactions to NSAIDs

Single-NSAID–induced urticaria/angioedema or anaphylaxis (SNIUAA): Immediate hypersensitivity reactions to a single NSAID or to several NSAIDs belonging to the same chemical class, presenting with urticaria, angioedema, and/or anaphylaxis. Patients typically tolerate NSAIDs from unrelated chemical classes and usually have no history of chronic urticaria or asthma. Historical terms include single-drug–induced reactions and allergic reactions.

Single-NSAID–induced delayed reactions (SNIDR): Hypersensitivity reactions to a single NSAID, typically developing within 24–48 hours after drug intake. Clinical manifestations include cutaneous symptoms (exanthema, fixed drug eruption), organ-specific involvement (e.g., kidney, lung), or severe cutaneous adverse reactions such as Stevens-Johnson syndrome.

Table 1. Novel classification of hypersensitivity reactions to NSAIDs. Reprinted from [7], with permission from John Wiley & Sons Ltd. © 2013 John Wiley & Sons A/S.

Type of reaction	Clinical manifestation	Timing of reaction	Underlying disease	Cross-reactivity	Putative mechanism	
NSAIDs-exacerbated respiratory disease (NERD)	Bronchial obstruction, dyspnea and/or nasal congestion/ rhinorrhea	Acute (usually immediate to several hours after exposure)	Asthma/ rhinosinusitis	Cross-reactive	Non-allergic	COX-1 inhibition
NSAIDs-exacerbated cutaneous disease (NECD)	Wheals and/or angioedema		Chronic urticaria			COX-1 inhibition
NSAIDs-induced urticaria/ angioedema (NIUA)	Wheals and/or angioedema		No			Unknown, probably COX-1 inhibition

Single-NSAID-induced urticaria/angioedema or anaphylaxis (SNIUAA)	Wheals/ angioedema/ anaphylaxis		No	Non-cross-reactive	Allergic	IgE-mediated
Single-NSAID-induced delayed reactions (SNIDR)	Various symptoms and organs involved (e.g., fixed drug eruption, SJS/TEN, nephritis)	Delayed onset (usually more than 24 h after exposure)	No			T-cell- mediated

Diagnosis of NSAID hypersensitivity should begin with a detailed clinical history, including the time of symptom onset, indication for drug use, brand name, dosage, route of administration, and concomitant medications [Figure 3]. The oral provocation test (OPT) remains the gold standard for confirming the diagnosis and should be performed in specialized centers, except in cases with severe delayed reactions, a history of severe anaphylaxis, uncontrolled chronic comorbidities (e.g., asthma, urticaria), poor pulmonary function, or conditions associated with high risk of deterioration. Skin testing may be useful only if a history suggests a SNIUAA. Several in vitro assays such as measurement of drug-specific IgE, cell activation tests (Basophil Activation Test Cellular Allergy Stimulation Test – CAST-ELISA) and Aspirin Sensitive Patient Identification Test (ASPITest) in acute form of reactions to NSAIDs and lymphocyte transformation test (LTT) in delayed reactions have been employed; however, none has yet been sufficiently validated for routine clinical practice [7].

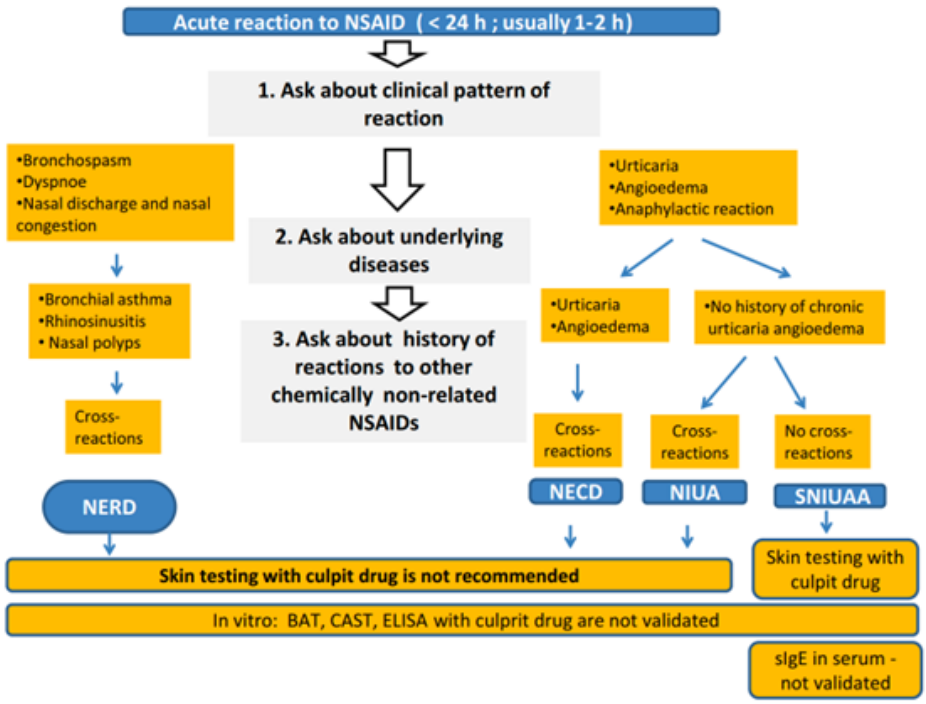

Figure 3. Algorithm for the diagnosis of acute forms of NSAID hypersensitivity. Reprinted from [7], with permission from John Wiley & Sons Ltd. © 2013 John Wiley & Sons A/S.

It is important to distinguish between aspirin hypersensitivity and aspirin intolerance, as they represent two distinct conditions with different underlying pathophysiological

mechanisms and hence require different clinical approaches. Adverse drug reactions are generally categorized into two types: type A ('augmented'), which are dose-dependent and predictable based on the pharmacological properties of the drug, and type B ('bizarre'), which are idiosyncratic and unpredictable. aspirin intolerance belongs to type A reactions, most commonly presenting with gastrointestinal symptoms (e.g., dyspepsia) or bleeding related to drug use. By contrast, aspirin hypersensitivity is a type B reaction, rare and unpredictable, occurring only in a subset of susceptible patients [8].

5. MANAGEMENT OF ASPIRIN HYPERSENSITIVITY IN PATIENTS WITH CAD

Currently, aspirin desensitization is considered the cornerstone strategy for managing hypersensitivity in patients with CAD. In addition, alternative therapeutic approaches to aspirin are being investigated to broaden treatment options. Accurate identification of the hypersensitivity phenotype is essential for determining the appropriate management strategy, including aspirin desensitization or the selection of a safe alternative agent. Figure 4 illustrates the diagnostic and therapeutic algorithm for different types of NSAIDs hypersensitivity [9].

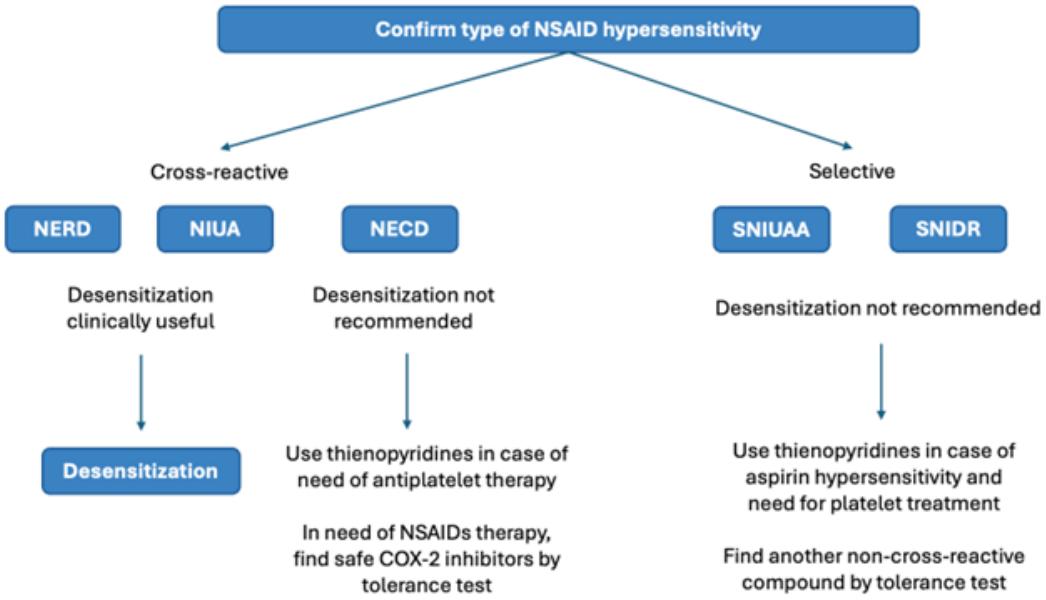

Figure 4. Algorithm for the management of different types of NSAID hypersensitivity. Adapted from [9], with permission from Springer Nature. © 2015 Springer International Publishing AG.

5.1. Aspirin desensitization

Aspirin desensitization involves the stepwise administration of gradually increasing doses of the drug with the aim of reducing or eliminating immunologically mediated reactions. Several desensitization protocols have been investigated, some extending over several days, which poses practical limitations in clinical use. Among the rapid desensitization strategies (completed within less than 6 hours), the protocol proposed by Rossini et al. in the ADAPTED (Aspirin Desensitization in Patients With Coronary Artery Disease) registry stands out, owing to the largest sample size (330 patients) and robust data on efficacy and safety [10].

The ADAPTED registry enrolled 330 patients with a self-reported history of aspirin hypersensitivity presenting with either an ACS or known/suspected CAD. Of these, 252 patients underwent desensitization before coronary angiography, while 78 patients with ST-segment elevation myocardial infarction (STEMI) received desensitization following emergency PCI. The protocol consisted of six sequential oral doses of aspirin (1, 5, 10, 20,

40, and 100 mg) administered over 5.5 hours. Vital signs were recorded every 30 minutes, and mucocutaneous, nasal–ocular and pulmonary reactions were closely monitored until 4 hours after completion of the protocol. The procedure was discontinued immediately if any signs of cutaneous, respiratory or systemic hypersensitivity occurred. Following successful desensitization, patients were maintained on aspirin 100 mg daily to prevent recurrence of hypersensitivity. The results demonstrated a success rate of 95.4% (315 of 330 patients), with 4.6% (15 of 330 patients) failing due primarily to cutaneous or respiratory reactions. At 12-month follow-up, 80.3% of patients continued aspirin therapy without delayed hypersensitivity reactions and the incidence of MACE was 11.8% [11].

Another study by Stéphane Manzo-Silberman et al. evaluated the efficacy of a rapid aspirin desensitization protocol in patients with aspirin hypersensitivity and concomitant CAD, focusing on platelet inhibition and basophil activation at day 1 and weeks 6–8 after desensitization. The findings demonstrated that aspirin achieved rapid biological efficacy, which was somewhat attenuated on day 1 but not significantly different from that of long-term aspirin users by weeks 6–8. However, persistent basophil activation several weeks after desensitization suggested an underlying propensity for hypersensitivity, thereby underscoring the need for continuous daily aspirin to maintain desensitization [12].

From a guideline perspective, in the setting of ACS, the 2025 ACC/AHA guidelines recommend aspirin desensitization whenever feasible in patients with a history of hypersensitivity, to enable initiation of dual antiplatelet therapy (DAPT) [1]. In contrast, for CCS, the 2024 ESC guidelines recommend clopidogrel as an alternative in patients intolerant to aspirin (Class I, LOE B). Prasugrel or ticagrelor monotherapy may be considered after PCI in cases where DAPT is not feasible due to aspirin intolerance (Class IIb, LOE C). Notably, aspirin desensitization protocols have not yet been incorporated as a formal therapeutic option in the management of CCS [13].

5.2. Alternative Strategies

In patients with a history of severe hypersensitivity reactions to aspirin or anaphylaxis, aspirin desensitization is contraindicated due to the risk of life-threatening events. Similarly, for patients in whom desensitization is unsuccessful, alternative therapeutic strategies must be considered. Although several approaches have been proposed, none have been formally endorsed in current clinical practice guidelines [10]. In Vietnam, the most common approach remains clopidogrel monotherapy in patients labeled as "aspirin allergic"; however, this strategy has notable limitations and is not considered fully optimal.

5.2.1. Cilostazol

Cilostazol, a cyclic adenosine monophosphate (cAMP)-dependent phosphodiesterase III inhibitor, exerts antiplatelet effects and has been approved in several Asian countries for secondary prevention of non-cardioembolic stroke. In a retrospective study conducted in China, cilostazol was compared with aspirin for efficacy and safety when combined with clopidogrel in patients intolerant to aspirin after PCI. Among 613 enrolled patients, 205 were aspirin-intolerant and received cilostazol 50 mg twice daily as a substitute. The results demonstrated no significant difference in major adverse cardiovascular events between the two groups ($p = 0.12$), with a trend toward reduced bleeding events in the cilostazol group (0.49% vs. 2.7%, $p = 0.063$) [14].

5.2.2. Dipyridamole

Dipyridamole is a long-established antiplatelet and coronary vasodilator that acts by inhibiting platelet phosphodiesterase and increasing interstitial adenosine levels. A nationwide case-control study in Taiwan compared combination therapy with dipyridamole plus clopidogrel versus clopidogrel monotherapy for secondary stroke prevention following MI in aspirin-intolerant patients. The results demonstrated that dipyridamole combined with clopidogrel did not improve event-free survival (composite of recurrent stroke, intracranial hemorrhage, gastrointestinal bleeding, or MI). Accordingly, this study did not support the use of dipyridamole in combination with

clopidogrel for secondary stroke prevention after MI [15].

5.2.3. Indobufen

Indobufen, an isoindolinyl phenyl-butyric acid derivative, exerts reversible antiplatelet activity by inhibiting TXA_2 production through COX-1 inhibition. A systematic review and meta-analysis including five studies with a total of 11,943 patients evaluated the efficacy of indobufen compared with aspirin. The results showed no statistically significant differences between the two groups in terms of composite vascular events, MI, ischemic stroke, or cardiovascular death at one year. Overall, the efficacy and safety profile of indobufen appeared comparable to aspirin monotherapy. Hence, indobufen may represent a reasonable alternative in patients intolerant or hypersensitive to aspirin; however, larger clinical trials are needed to confirm its broader applicability [16].

5.2.4. Rivaroxaban

The combination of an oral anticoagulant with a P2Y12 inhibitor (most commonly clopidogrel) may represent another alternative strategy. The GEMINI-ACS-1 trial evaluated the safety of low-dose rivaroxaban (2.5 mg twice daily) compared with aspirin (100 mg daily), each combined with a P2Y12 inhibitor (clopidogrel or ticagrelor), in patients with ACS within 10 days of hospitalization. The results showed that low-dose rivaroxaban in combination with a P2Y12 inhibitor was associated with a similar bleeding risk compared with standard DAPT. However, the trial was not powered to assess ischemic efficacy, highlighting the need for additional phase III studies to confirm these findings [17].

In summary, several aspirin alternatives have been investigated, including cilostazol, dipyridamole, indobufen, and low-dose rivaroxaban in combination with a P2Y12 inhibitor. Table 2 provides a comparative overview of the key features of these alternatives to aid individualized treatment strategies. Nevertheless, substantial gaps in evidence remain. To date, no large-scale RCT has directly compared alternative strategies in patients unable to receive aspirin. Consequently, the optimal approach to balance ischemic protection against bleeding risk remains unresolved. High-quality future RCTs are warranted to establish a robust evidence base and inform guideline recommendations for this unique patient population.

Table 2. Aspirin alternatives in patients with CAD intolerant or hypersensitive to aspirin

Drug	Advantages	Limitations	Current evidence
Cilostazol	- PDE-III inhibition with antiplatelet and vasodilatory effects - Widely used in secondary stroke prevention in Asia - Retrospective data: comparable efficacy to aspirin and lower bleeding risk when combined with clopidogrel	- Evidence largely based on small retrospective studies - No large RCTs in ACS - Adverse effects: headache, palpitations, diarrhea	Retrospective studies (China)
Dipyridamole	- Dual mechanism: platelet PDE inhibition and increased adenosine levels - Longstanding and familiar in clinical use	- Case-control study: no improvement in event-free survival when combined with clopidogrel - Not recommended for secondary prevention post-MI - Adverse effects: headache, flushing, hypotension	Nationwide case-control study (Taiwan); not supportive of clopidogrel combination

Indobufen	- Reversible COX-1 inhibition, reducing TXA_2 - Comparable efficacy and safety to aspirin monotherapy - Potential alternative in aspirin-intolerant patients	- Limited availability outside Italy/China - Lack of data in ACS populations - Larger confirmatory RCTs needed	Meta-analysis of 5 studies (~11,943 patients)
Low-dose rivaroxaban (2.5 mg twice daily)	- GEMINI-ACS-1: safety comparable to aspirin when combined with a P2Y12 inhibitor - Potential alternative strategy in ACS - Possible benefit in high thrombotic-risk patients	- Phase II study; not powered to assess ischemic efficacy - No phase III RCT confirmation - Bleeding risk remains a concern	GEMINI-ACS-1 (Phase II)

6. CONCLUSION

Aspirin hypersensitivity represents a major challenge in the management of CAD, given aspirin's central role in thromboprophylaxis and secondary prevention of cardiovascular events. Current evidence supports aspirin desensitization as the preferred strategy whenever feasible, particularly in the setting of ACS. For patients with a history of severe anaphylaxis or in whom desensitization fails, alternative strategies—including clopidogrel, indobufen, cilostazol, or a regimen combining a P2Y12 inhibitor with low-dose rivaroxaban—may be considered, but decisions should be individualized according to the balance between ischemic and bleeding risks. Despite the exploration of several alternative approaches, the existing evidence remains limited and practice recommendations are not yet standardized, especially in resource-limited settings such as Vietnam. These gaps underscore the urgent need for large-scale RCTs and real-world data to establish optimal management strategies for aspirin-hypersensitive patients with CAD.

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