

UDC 616.1:616-002:577.15

DOI: <http://doi.org/10.31928/2664-4479-2025.6.4149>

Linking inflammation and cardiovascular disease: the emerging role of lipoprotein-associated phospholipase A₂

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Over the past decades, inflammation has been recognized as a key contributor to the development of atherosclerosis, prompting extensive research. Numerous inflammatory markers have demonstrated predictive value for both initial and recurrent coronary events in individuals with or without established coronary vascular disease (CVD). Among these, lipoprotein-associated phospholipase A₂ (Lp-PLA₂) has garnered significant attention. Lp-PLA₂ may be involved in the atherosclerotic process and contribute to plaque destabilization through its inflammatory activity within atherosclerotic lesions. Lipoprotein-associated phospholipase A₂ (Lp-PLA₂), a recently identified cardiovascular-specific inflammatory mediator, is closely associated with the onset and progression of cardiovascular events. This review explores the potential of Lp-PLA₂ as both a risk marker and a therapeutic target in CVD. Elevated levels of Lp-PLA₂ mass and activity have been linked to an increased risk of CVD in both the general population and patients with pre-existing disease. However, it remains uncertain whether incorporating Lp-PLA₂ measurements into risk prediction models significantly enhances risk stratification beyond traditional cardiovascular risk factors. Additionally, the failure of darapladib, a potent and selective Lp-PLA₂ inhibitor, to reduce CVD events in major randomized, placebo-controlled trials suggests the importance of ongoing research to fully understand its functions and develop effective strategies for CVD prevention and treatment.

Key words: coronary vascular disease, lipoprotein-associated phospholipase A₂, atherosclerosis, inflammation.

Cardiovascular diseases (CVDs) continue to be the leading cause of death worldwide. Despite significant improvements in medical treatments over recent decades, it is widely acknowledged that inflammatory responses play a crucial role in the development of atherosclerosis, from the initial formation of atherosclerotic plaque to its eventual instability and rupture. Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) is strongly associated with an elevated risk of CVD development. Lp-PLA₂ may contribute to plaque destabilization and be a component of the atherosclerotic process through inflammatory activity within atherosclerotic lesions. However, each attempt to convert phospholipase inhibition into clinically

advantageous CVD risk reduction, including in randomized trials via Lp-PLA₂ inhibition by darapladib, unexpectedly failed. This makes it extremely important to keep researching to learn more about how Lp-PLA₂ controls vascular inflammation and the formation of atherosclerotic plaque. For the present review, a search was conducted on PubMed and ScienceDirect. This article summarizes the literature data on the association between Lp-PLA₂, inflammation, and CVD, encompassing 29 articles published between 2015 and 2024. Establishing and validating current and new anti-inflammatory therapeutic approaches is necessary from a clinical perspective to prevent the development of CVD. Lp-PLA₂ is a relatively new inflammatory

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Стаття надійшла до редакції 27 жовтня 2025 року

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Received on 27.10.2025

marker, and the effect of Lp-PLA₂ in atherosclerosis remains controversial, however, increasing evidence suggests that it plays a significant role in the development of coronary atherosclerosis. Plenty of studies show that Lp-PLA₂ activity is positively correlated to the seriousness of CVD, and this can provide a strong basis for predicting the occurrence and prognosis of CVD, at the same time, it may provide a new way to treat CVD in the future [1].

Biochemical properties of lipoprotein-associated phospholipase A₂

Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) was first discussed in 1980. Lp-PLA₂ is encoded by the phospholipase A₂ group VII (PLA2G7) gene. Lp-PLA₂ is a 45-kDa hydrophobic calcium-independent protein with 441 amino acids [2]. It can catalyze hydrolysis at the phospholipid sn-2 location, and sequence analysis showed that the main structure of Lp-PLA₂ has the Gly-Xaa-Ser-Xaa-Gly (GX SXG) motif, which is the distinctive fingerprint for neutral lipases and serine esterases. As a result, Lp-PLA₂ possesses traits of neutral lipases as well as PLA₂s. Although hematopoietic cells may be the primary source of circulating Lp-PLA₂ levels, several organs appear to be additional sources, including liver cells, aorta cells, and adipocytes. Following secretion, Lp-PLA₂ travels through the bloodstream by attaching itself to lipoproteins. LDL and HDL account for 70 % to 80 % and 20 % to 30 % of the total plasma activity, respectively. Since Lp-PLA₂ does not exhibit any indications of interfacial activation, it operates on the substrate in the aqueous phase. As is the case with all common membrane-associating PLA₂ enzymes, we cannot completely rule out the potential that Lp-PLA₂ will bind to its substrates from the lipid membrane phase because the surfaces of both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) are loaded with phospholipids. Another remarkable characteristic of Lp-PLA₂, given its increased production in response to oxidative stress, is its vulnerability to oxidative inactivation. Irreversible alteration of important amino acid residues may be involved in the suppression of Lp-PLA₂ activity, which appears to be caused by both physiological (heavy metals and oxygen radicals) and nonphysiological (cigarette smoke) oxidants. It was discovered that Lp-PLA₂ is inactivated by peroxynitrite, one of the main oxidants generated during cellular oxidation *in vivo*. Used site-directed mutagenesis to show that Met117, which was exposed on the protein surface, was the main target of oxidation in the protein. Oxidation of this protein would not only cause enzymatic inactivation but also alter its association with LDL. Furthermore, tyrosine nitration of Tyr307 and Tyr335 also played a moderate role in the enzyme's deactivation. To clarify the impact

of the structural modification of Lp-PLA₂ on the oxidation of the three amino acids indicated above, we recently employed essential dynamics and molecular dynamics simulation in conjunction with a molecular docking technique. According to the findings, Met117 oxidation resulted in increased flexibility, less compactness when oxidized, and little binding to the PAF substrate. In addition to the substrate's lower binding affinity and increased flexibility, nitration of Tyr307 and Tyr335 caused the catalytic triad to become disoriented and NT-Tyr307 and NT-Tyr335's molecular interactions with other protein residues to decrease. Although these results provided a reasonable explanation for the decrease in Lp-PLA₂ enzymatic activity under oxidative stress, more research employing other biophysical methods, including nuclear magnetic resonance, cryoelectron microscopy, and X-ray crystallography, is expected to shed more light on the molecular mechanisms [3].

Proinflammatory and atherosclerotic effects of Lipoprotein-associated phospholipase A₂

Lp-PLA₂ is capable of hydrolyzing the acetyl group at PAF's sn-2 (stereo-specifically numbering-2) position. It was initially identified as a platelet-activating factor (PAF) acetylhydrolase characterized by a distinctive GX SXG motif commonly associated with lipases. Several inflammatory cells, such as mast cells, T cells, and monocytes/macrophages, express Lp-PLA₂. About 80 % of Lp-PLA₂ in humans circulates after secretion by attaching to LDL. The remaining 20 % is coupled to HDL. Lysophosphatidylcholine (LPC) and oxidized free fatty acids (oxFFAs), two downstream metabolites of Lp-PLA₂ produced during the hydrolysis of polar phospholipids (phosphatidylcholine) on oxLDL (oxidized LDL), appear to exert a variety of proinflammatory and proapoptotic effects (*Figure 1*). Elevated Lp-PLA₂ levels have been linked to a higher risk of atherosclerosis [4, 5]. In humans, Lp-PLA₂ serves two main purposes. First of all, it functions as an antioxidant. In the inner layer of the blood vessel wall, macrophages, mast cells, and T cells release Lp-PLA₂, which is present in the blood along with LDL. Lp-PLA₂ can hydrolyze its oxidative component when the organism is experiencing oxidative stress, leading to partial oxidation of LDL. Second, it has a well-established impact of triggering inflammation. Endothelial dysfunction increases vascular permeability and promotes monocyte adhesion and transmigration into the intima. The endothelium structural and functional alterations facilitate leukocyte entry and retention within the subendothelial space. Macrophages, mast cells, and T cells will release more Lp-PLA₂ while under oxidative stress. Additionally, the intima's macrophages will

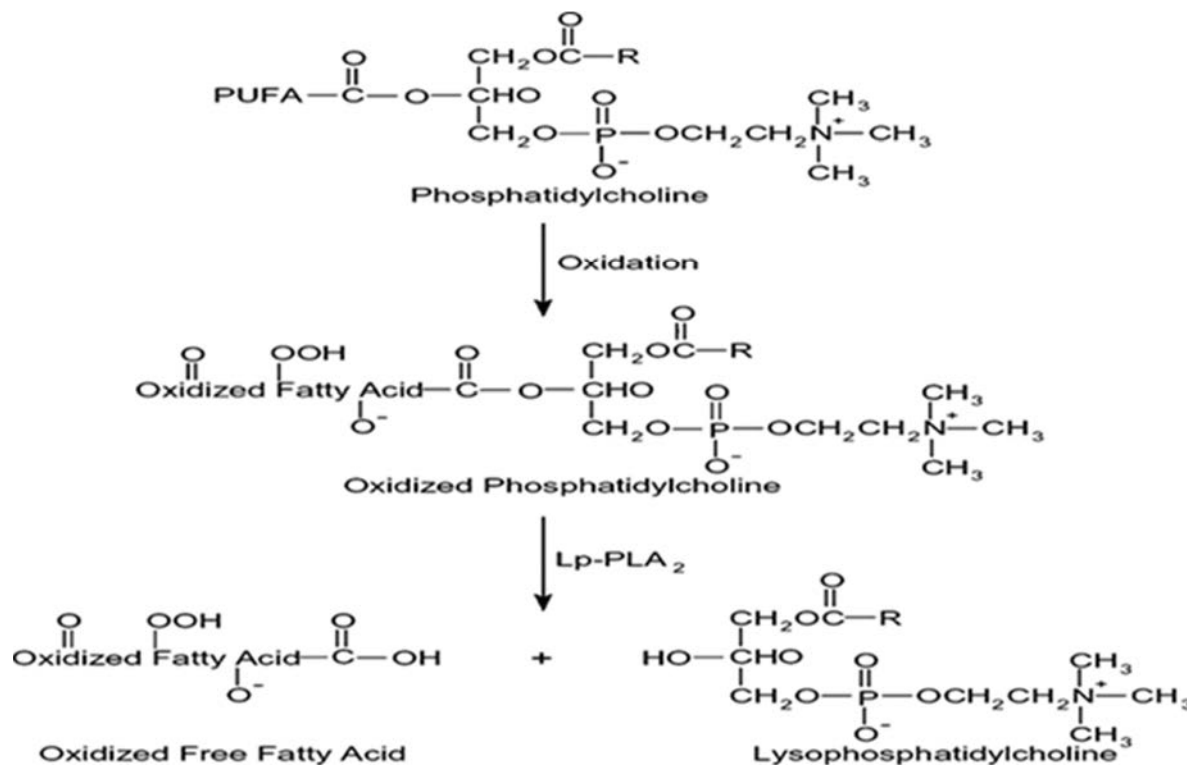


Figure 1. The catalytic action of Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) on oxidized phosphatidylcholine to produce oxidized free fatty acids (oxFFA) and Lysophosphatidylcholine (LPC).

absorb oxidized LDL and transform into foam cells, promoting the formation of plaque and increasing the risk of a cardiovascular event. There is a clear association between the state of inflammation and Lp-PLA₂. Inflammation and metabolic syndrome are also recognized to be related. Modern lifestyles have made metabolic syndrome a serious public health issue. Apart from diabetes and cardiovascular disease, metabolic syndrome is also linked to the development of chronic organ illnesses. Moreover, in people with metabolic syndrome, it raises the body's production of inflammatory cytokines and reactive oxygen species and ultimately puts it under oxidative stress. Raising the degree of insulin resistance also causes adipocyte hypertrophy and macrophage accumulation to reduce the inflammatory state. Lp-PLA₂ contributes to inflammation both locally within the plaque and systemically. Locally, its hydrolytic activity on oxidized LDL generates LPC and oxFFAs, which promote endothelial activation, monocyte recruitment, and smooth muscle cell migration, ultimately accelerating necrotic core formation. Systemically, elevated Lp-PLA₂ levels in metabolic syndrome amplify chronic low-grade inflammation by increasing LPC-mediated cytokine release and enhancing circulating atherogenic lipoprotein modifications [6, 7].

Role of Lipoprotein-associated phospholipase A₂ in the development of cardiovascular diseases

Atherosclerosis, which includes endothelial dysfunction, inflammation, oxidative stress, insulin resistance, and dyslipidemia, is a hallmark of the pathophysiology of CVD. Elevated levels of Lp-PLA₂ have been consistently linked to an increased risk of CVD. The American College of Cardiology still projects that there will be 25 million instances of CVD in the USA alone by the end of 2050, despite early identification and improved treatment options. Additionally, considering the current significance of CVD, which accounts for around 30 % of all fatalities worldwide due to its high incidence, monitoring novel biomarkers and risk variables is a key area of attention for new research [8]. Endothelial dysfunction occurs before atherosclerosis develops and contributes to the early and late mechanisms of progression. LDL particles can more readily transmute to the artery intima because of their characteristics, which include increased endothelial permeability and the expression of more adhesion molecules. LDL particles are subject to further oxidation due to the artery intima's decreased antioxidant capacity. Thus, OxLDL contains a large amount of oxidized

phospholipids, which activate Lp-PLA₂. Therefore, it can be said that the Lp-PLA₂-driven hydrolysis of the oxidized phospholipids limits the changes of OxLDL to some degree and serves a protective purpose. According to specific research, compared to non-carriers, people with loss-of-function (V279F) mutations may have a higher incidence and severity of cardiovascular diseases. The V279F mutation leads to misfolding of the Lp-PLA₂ protein, preventing its secretion and resulting in almost complete loss of enzymatic activity in plasma. Nonetheless, most research supports the idea that Lp-PLA₂ plays a role in the onset and progression of atherosclerosis. The fundamental explanation is that OxFFA and LPC are generated after Lp-PLA₂-enhanced phospholipid hydrolysis. These substances stimulate the production of cytokines (Tumor Necrosis Factor- α (TNF- α), Interleukin-6 (IL-6)), attract macrophages to the arterial intima, and promote the expression of adhesion molecules [9].

Since recruiting more inflammatory cells in activated plaques may lead to increased Lp-PLA₂ synthesis and activity, a detrimental feed-forward mechanism may also be involved. Lp-PLA₂ is further produced by foam cells and activated macrophages. Darapladib is one of the Lp-PLA₂ inhibitors that could reduce the elevated Lp-PLA₂ activity in atherosclerosis (Figure 2) [10, 11].

Numerous epidemiological and clinical studies suggest that Lp-PLA₂ is a valuable biomarker for cardiovascular risk stratification. The study by Zhang found that the level of Lp-PLA₂ increased in line with the number of diseased coronary branches. The levels of Lp-PLA₂ in the patients with CVD (Acute Myocardial Infarction – AMI and Unstable angina – UA) were higher when compared with the control and Stable angina (SA) groups. Lp-PLA₂ had 75.6 % sensitivity and 67.3 % specificity for recognizing CVD, and 53.0 % sensitivity and 80.3 % specificity for recognizing severe CVD. Thus, the activity of Lp-PLA₂ positively correlated with the seriousness of CVD [1]. In one case-control study, circulating plasma Lp-PLA₂ was found to be elevated in the CVD group in Asian Indians compared to the control group [12]. In the review article of Li, greater Lp-PLA₂ activity or mass was independently associated with cardiovascular events in patients with CVD, particularly in patients with stable CVD who were not receiving therapies for inhibiting Lp-PLA₂ [13]. A meta-analysis involving 15 studies and more than 30,000 subjects confirmed that higher Lp-PLA₂ activity or quality was independently associated with cardiovascular events in patients with stable coronary atherosclerotic heart disease who were not treated with Lp-PLA₂ inhibition [14]. The study of Lp-PLA₂ levels may help in the early identification of risk and thus

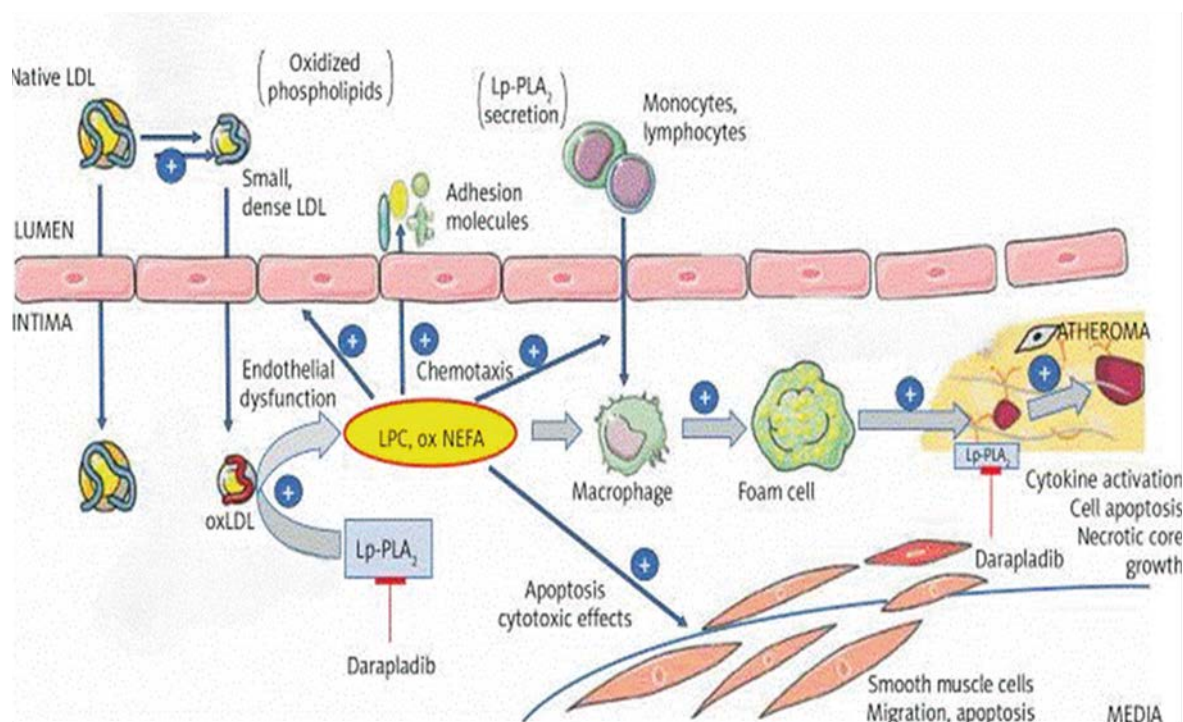


Figure 2. Schematic presentation of the role of Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) in atherogenesis, and the potential sites for therapeutic inhibition, by using a specific Lp-PLA₂ inhibitor – darapladib. Adapted from: Fras Z, Tršan J, Banach M. On the present and future role of Lp-PLA₂ in atherosclerosis-related cardiovascular risk prediction and management. Arch Med Sci. 2020 Aug 20;17(4):954-964. doi: 10.5114/aoms.2020.98195.

may play a beneficial role in the proactive management of COVID-19 [15]. Recent studies have investigated the diagnostic value of Lp-PLA₂ in CVD. Findings suggest that measuring plasma levels of Lp-PLA₂, alongside other biomarkers like homocysteine, can enhance the accuracy of CVD diagnosis [16]. In a recent study were examined 208 patients with chronic ischaemic heart disease were examined, and the variation of Lp-PLA₂ serum concentration values was analysed dynamically at a two-week interval. It was found that the values of serum concentration of Lp-PLA₂ can be accepted as a biomarker with diagnostic specificity for chronic ischaemic heart disease, both in situations where the patient, although clinically reporting the existence of angina pectoris, does not show specific changes on an EKG, and for the assessment of the response to personalised therapy [17]. A novel review describes that total plasma Lp-PLA₂ was identified as a predictor of cardiac mortality in a cohort of 524 patients from Athens with stable CVD, followed over an average of 34 months. In a study involving 224 African Americans and 336 Caucasians undergoing coronary angiography, both Lp-PLA₂ activity and index (a combined measure of mass and activity) were linked to the presence of CVD. The findings highlighted an independent role of vascular inflammation in African Americans contributing to CVD risk and emphasized the relevance of Lp-PLA₂ as a cardiovascular risk marker. Similarly, a nested case-control study among American Indians with high insulin resistance and diabetes showed a correlation between Lp-PLA₂ and CVD events. The study also noted a negative association between Lp-PLA₂ quality and CVD outcomes. Another investigation involving 25 Turkish patients with isolated coronary artery ectasia (CAE) and 25 healthy controls found significantly elevated Lp-PLA₂ levels in the CAE group, suggesting a potential role of Lp-PLA₂ in CAE pathogenesis [18]. In a group of 4,537 U.S. participants without peripheral artery disease (PAD) at baseline, increased Lp-PLA₂ quality and activity were associated with the onset of PAD events [19]. Among 929 Japanese men aged 50–79 years, higher Lp-PLA₂ activity was significantly linked to greater carotid intima-media thickness (IMT) and plaque presence. However, a Mendelian randomization analysis did not support a causal relationship between Lp-PLA₂ and subclinical atherosclerosis [20]. A Quebec-based study on 183 patients with mild aortic stenosis (AS) found that elevated Lp-PLA₂ activity correlated with more rapid disease progression, though no such link was observed in moderate or severe AS cases [21]. Furthermore, Lp-PLA₂ activity was significantly related to CVD among men and women with type 2 diabetes [22]. On the other hand, some studies reported contradictory findings. In 819 participants from the Framingham Offspring study (average age 73), no significant association was found between Lp-PLA₂ levels

and cerebral microbleeds (CMB). A cross-sectional study involving 921 non-stroke patients in Barcelona found that while Lp-PLA₂ was independently associated with silent cerebral infarction in women, adding it to clinical predictors did not enhance predictive accuracy. Similar inconsistencies appeared in studies involving Chinese populations. While many identified Lp-PLA₂ as a risk factor for cardiovascular and cerebrovascular diseases, one study in northern China showed a positive association between Lp-PLA₂ quality and subclinical atherosclerosis (assessed through asymptomatic cerebral artery stenosis, including intracranial arterial stenosis (ICAS) and extracranial arterial stenosis (ECAS)), particularly among older males. This supports the idea that Lp-PLA₂ could serve as a biomarker for detecting adults with asymptomatic carotid artery stenosis (aCAS). In the Chinese Acute Ischemic Stroke Blood Pressure Reduction Trial, a prospective analysis of 3,401 participants revealed that all-cause mortality rates increased across higher quartiles of Lp-PLA₂ quality [23]. However, a multicenter randomized clinical trial found no increase in Lp-PLA₂ activity in patients without intracranial artery stenosis, suggesting that those individuals may benefit more from dual antiplatelet therapy to prevent strokes and other vascular events. Another Chinese randomized controlled trial indicated that elevated Lp-PLA₂ activity during the acute phase of stroke was associated with a higher risk of short-term recurrent vascular events. Nevertheless, a large 7-year follow-up study involving 90,000 Chinese participants found that reductions in Lp-PLA₂ activity did not significantly impact the risk of vascular or nonvascular diseases [18]. Another study showed that Lp-PLA₂ mass level was higher in patients with acute ischemic stroke (AIS) and linked with underlying poor cardio-metabolic disorders. Therefore, the Lp-PLA₂ mass level is observed to be a surrogate biomarker of acute ischemic stroke, mainly in patients with poor cardio-metabolic disorders. Statins therapy improves the Lp-PLA₂ mass level and the poor cardio-metabolic profile in patients with acute ischemic stroke [24].

Role of Lipoprotein-associated phospholipase A₂ in coronary plaque formation and progression

Coronary atherosclerosis and unstable vascular plaques can lead to plaque rupture or erosion when triggered by various factors. This process often results in coronary thrombosis and partial or complete blockage of the affected blood vessels, ultimately causing acute myocardial ischemia and oxygen deprivation. The onset of acute coronary syndrome (ACS) is mainly determined by the stability of the plaque rather than its size [25]. Inflammation contributes to all stages of the

atherosclerotic plaque life cycle. Importantly, non-resolving inflammation induces the development of unstable atherosclerotic plaques by promoting sustained plaque pathology and the formation of large necrotic cores and thin fibrous caps, ultimately leading to plaque rupture [26]. The correlation of Lp-PLA₂ with atherogenic risk is even greater, considering that the macrophages of the atherosclerotic plaques secrete it and may well represent the transition to plaque instability. Lp-PLA₂ protein is localized within the plaque in high concentrations during arterial wall inflammation. The increase in Lp-PLA₂ levels is associated with atherosclerotic plaque rupture and blood clot production, which may cause cardiovascular events. The recruitment of inflammatory cells and the release of inflammatory mediators are key contributors to the development and progression of atherosclerotic plaques. Lipoprotein-associated phospholipase A₂ (Lp-PLA₂), a newly discovered inflammatory marker, plays an important role in the occurrence and development of atherosclerosis and the rupture of unstable plaques. The rupture of unstable plaques is crucial to the occurrence of ACS [27]. Moreover, another study showed that increased intracoronary Lp-PLA₂ secretion correlated strongly with intracoronary dysfunction and the atheromatous volume of coronary plaques [9]. In atherosclerotic plaques, Lp-PLA₂ hydrolyzes and oxidizes LDL, generating metabolites that trigger an inflammatory response, which leads to endothelial dysfunction,

necrosis, and apoptosis. This cascade contributes to the progression of atherosclerosis and the destabilization of plaques. OxLDL, OxFFA, and LPC promote plaque growth and ultimately result in the development of a necrotic core. They can also determine the likelihood of plaque rupture, leading to a cardiovascular event. Thin-cap fibroatheromas and ruptured plaques have high quantities of Lp-PLA₂ and lysophospholipids, whereas stable lesions have nearly no levels of these substances [10]. Lp-PLA₂ is a particular marker for inflammation in plaques, making its measurement a more accurate indicator of plaque stability than traditional, less specific inflammatory markers like high sensitive C-reactive protein (hs-CRP) and IL-6 [28]. Plasma Lp-PLA₂ activity reflects systemic pro-atherogenic lipoprotein burden but only partially corresponds to intraplaque Lp-PLA₂ levels, as vascular-wall Lp-PLA₂ is predominantly produced by macrophages within the lesion. Thus, circulating measures serve as indirect risk markers rather than precise indicators of local enzymatic activity. The mechanism by which Lp-PLA₂ affects atherosclerotic plaques involves its hydrolysis of oxidized phosphatidylcholine, leading to the production of LPC and oxFFAs. These metabolites act as inflammatory mediators, enhancing the expression of adhesion molecules, cytokines, and CD40 ligand. They also stimulate the proliferation of macrophages, increase production of monocyte chemoattractant protein-1, promote smooth muscle cell (SMC)

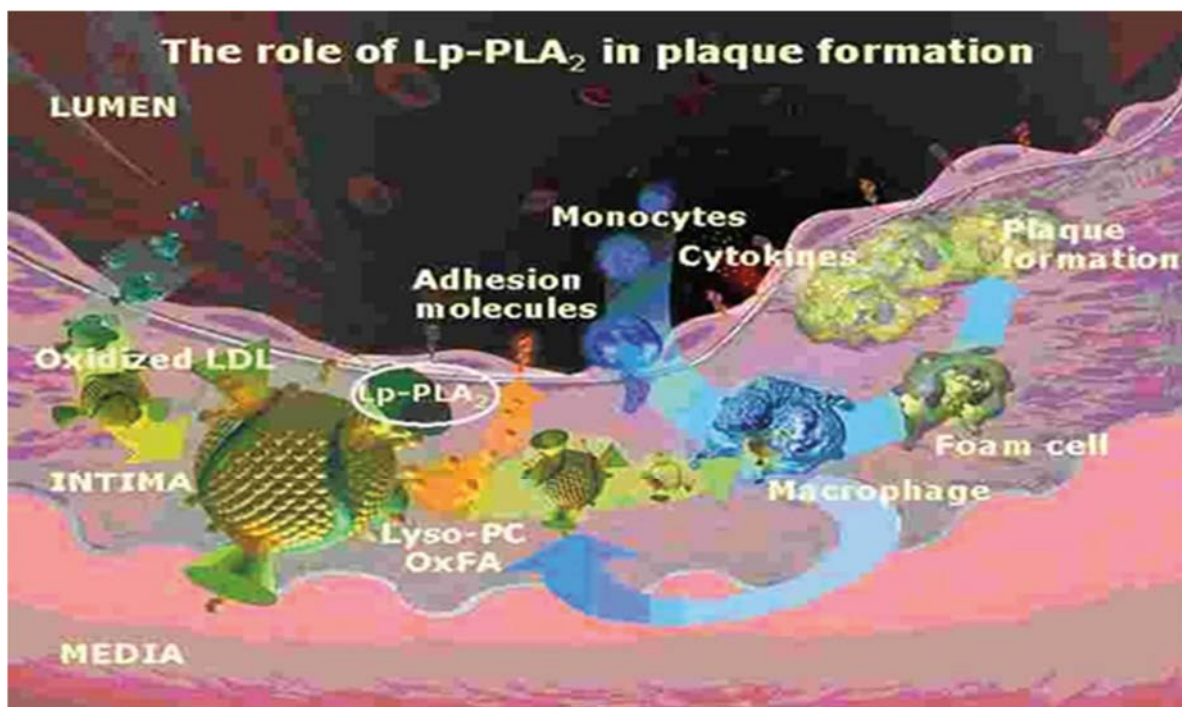


Figure 3. **The proposed role of Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) in atherosclerotic plaque formation.** Adapted from: McConnell JP, Hoefner DM. Lipoprotein-associated phospholipase A₂. Clin Lab Med. 2006 Sep;26(3):679-97, vii. doi: 10.1016/j.cll.2006.06.003.

migration, and reduce the availability of endothelial-derived nitric oxide. In this way, Lp-PLA₂'s activity on oxLDL particles in the vessel wall generates LPC and oxFFAs, which trigger vascular inflammation, attract monocytes, and promote apoptosis in the plaque. As a result, macrophages engulf the oxLDL in the vessel wall, forming foam cells that contribute to the lipid core. Additionally, macrophages produce more Lp-PLA₂, sustaining the process [29]. This cycle is central to the formation and progression of atherosclerotic plaques and is presented in *Figure 3*.

Lipoprotein-associated phospholipase A2 as a potential therapeutic target

Lp-PLA₂ is a potential therapeutic target due to its function in atherosclerosis-related inflammation. Darapladib is one of the Lp-PLA₂ inhibitors developed to investigate their efficiency in reducing cardiovascular events. Inhibitors of Lp-PLA₂ have been developed to reduce vascular inflammation and subsequent cardiovascular events. However, clinical trials have yielded

There is no conflict of interest.

Authors contributions: study concept and design – I.K., K.T.T.; data collection and analysis – I.K., H.A.; writing – I.K.; critically review of the text – K.T.T.; final approval – I.K., H.A., K.T.T.

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mixed results regarding their efficacy, indicating the need for further research to elucidate the therapeutic benefits and safety of Lp-PLA₂ inhibition. In a large-scale human genetic study, none of a series of Lp-PLA₂-lowering alleles was related to coronary heart disease risk, suggesting that Lp-PLA₂ is unlikely to be a causal risk factor [30]. Further research is needed to fully understand the therapeutic potential of Lp-PLA₂ inhibition, as clinical trials have yielded mixed results.

Conclusions

Lp-PLA₂ is a crucial link between lipid metabolism and inflammation, contributing to the development of atherosclerosis and cardiovascular disorders. Its potential as a biomarker for cardiovascular risk stratification and therapeutic target remains a topic of intensive investigation. Its role as both a biomarker and a potential therapeutic target underscores the importance of ongoing research to fully understand its functions and to develop effective strategies for CVD prevention and treatment.

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Зв'язок між запаленням і серцево-судинними захворюваннями: нова роль ліпопротеїн-асоційованої фосфоліпази A₂

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За останні десятиліття запалення було визнано ключовим чинником розвитку атеросклерозу, що стимулювало проведення масштабних досліджень. Багато маркерів запалення продемонстрували прогностичну цінність як для первинних, так і для повторних коронарних подій в осіб із серцево-судинним захворюванням (ССЗ) або без нього. З-поміж них значну увагу привернула ліпопротеїн-асоційована фосфоліпаза A₂ (Lp-PLA₂). Вважається, що Lp-PLA₂ може бути залучена до атеросклеротичного процесу та сприяти дестабілізації бляшок через свою запальну активність у ділянці атеросклеротичного ураження. Lp-PLA₂, як нещодавно ідентифікований серцево-судинний специфічний медіатор запалення, тісно пов'язана з виникненням і прогресуванням серцево-судинних подій. У цьому огляді розглянуто потенціал Lp-PLA₂ як фактора ризику і терапевтичної мішені при ССЗ. Підвищені рівні та збільшена активність Lp-PLA₂ пов'язані зі зростанням ризику ССЗ як у загальній популяції, так і в пацієнтів, що вже мають захворювання. Однак незрозуміло, чи може використання показників рівня та активності Lp-PLA₂ суттєво підвищити стратифікацію ризику в моделях оцінки ризику розвитку ССЗ у пацієнтів порівняно з традиційними серцево-судинними факторами.

Крім того, відсутність ефективності дарапладибу (darapladib) — потужного селективного інгібітора Lp-PLA₂ — у зниженні частоти серцево-судинних подій у великих рандомізованих плацебоконтрольованих дослідженнях підкреслює важливість подальших досліджень для повного розуміння його функцій і розроблення ефективних стратегій профілактики й лікування ССЗ.

Ключові слова: серцево-судинні захворювання, ліпопротеїн-асоційована фосфоліпаза A₂, атеросклероз, запалення.