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Emerging Biomarkers in Atherosclerosis: Advancing Early Detection and Risk Stratification

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Abstract:

Introduction:

Atherosclerosis is a complex, multifactorial disease influenced by both genetic and environmental factors, including obesity, cigarette smoking, excessive alcohol consumption, and certain chronic conditions such as hypertension and diabetes mellitus type 2. The disease progresses gradually, and often remains unnoticed for years until serious health complications such as coronary artery disease (CAD), peripheral artery disease (PAD) or cerebrovascular disease arise.

Nowadays, the diagnosis of atherosclerosis relies on the identification of specific biological markers, enabling early detection and assessment of disease progression. The most common markers used in clinical practice include low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TGs), and lipoprotein(a) (Lpa). However, considering that atherosclerosis is one of the leading causes of mortality worldwide and its etiology still remains insufficiently elucidated, there is a pressing need for new, more specific biomarkers for its earlier detection.

Aim of the study:

The aim of this study is to summarize the knowledge concerning new potential biomarkers for the early detection of atherosclerosis through analyzing the biological processes associated with the initiation and progression of the disease, such as inflammation, oxidative stress, and endothelial dysfunction, to better understand its pathophysiology.

Materials and methods:

A systematic review of scientific and medical literature from the PubMed and Google Scholar databases was conducted.

Results:

The analysis of available studies indicates that there are numerous potential biomarkers that might be used for the early diagnosis of atherosclerosis, such as molecules associated with inflammation, lipid oxidation, or endothelial damage. However, further research is needed to establish their full clinical utility.

Conclusions:

Advances in identifying new biomarkers for atherosclerosis offer new opportunities for diagnosing, prognosing, and monitoring the disease. These biomarkers, reflecting pathomechanisms involved in the disease development namely endothelial dysfunction, inflammation, and thrombotic complications, could complement currently assessed bio markers and risk factors. While early studies show promise, large-scale research is needed to confirm their clinical utility, including their specificity, sensitivity, and role in risk assessment. In the future, these markers or even their panels may enable more accurate risk evaluation, improved disease monitoring, and implementation of personalized therapies, ultimately enhancing patients' outcomes. However, further assessment of their specificity, sensitivity and cost-effectiveness is needed to establish their potential in everyday medical practice.

Key words: atherosclerosis, biomarkers, lipoproteins, cardiovascular disease

1. Introduction:

Atherosclerosis is a complex, multifactorial, chronic disease that affects the middle- and large-sized arteries throughout the body [1]. Complications resulting from atherosclerotic disease such as coronary artery disease (CAD), ischemic stroke or peripheral artery disease (PAD) are responsible for high morbidity and death rates in industrialized societies. In spite of significant progress in understanding the pathophysiology and improvements in pharmacotherapy through the last few years, atherosclerotic disease still remains one of the burning issues in healthcare systems worldwide [2].The pathogenesis of atherosclerosis can be divided into several stages: the accumulation of lipoproteins, especially LDL, under the intimal layer of arteries, activation of the inflammatory process and platelets, neurohormonal disturbances, and shear stress in the vascular endothelium [3].

According to current studies, plasma level of low density lipoprotein cholesterol (LDLC) plays a crucial role in the pathogenesis of atherosclerosis [4]. An atherosclerotic lesion consists of a lipid core and a fibrous cap which divides the core from arterial lumen. One of the earliest manifestations of atherosclerotic disease is related to the deposition of lipids in the arterial intimal layer. Within intima, lipids gather not only inside the vascular wall cells but also in the extracellular space where they are linked with the components of the extracellular matrix.Next, macrophages begin to absorb LDL-C, leading to the formation of foam cells, which are crucial in the development of atherosclerotic plaques. Those cells are filled with droplets [5].

Inflammation also plays a pivotal role in the pathogenesis of atherosclerosis, serving as a driver process in the development and progression of atherosclerotic changes. The formation of an atherosclerotic plaque begins with vascular endothelial damage, leading to increased permeability of low-density lipoproteins (LDL) into the vessel wall and their oxidation [6]. Modified LDL triggers an inflammatory response by activating endothelial cells and recruiting monocytes, which differentiate into macrophages that engulf lipids and form foam cells [7]. The production of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as the presence of growth factors, stimulates the proliferation of smooth muscle cells (SMCs) and the deposition of extracellular matrix [8]. Chronic inflammation promotes plaque destabilization, making it more prone to ruptures, which can result in complications such as myocardial infarction or stroke [9]. Modern anti-atherosclerotic therapies increasingly focus on modulating inflammation to reduce cardiovascular risk [10].

An additional process involved in the pathogenesis of atherosclerosis, particularly in its advanced stages, is thrombocyte activation. This process is initiated by vascular endothelial damage, which leads to the exposure of subendothelial structures such as collagen and tissue factors [11]. This exposure promotes the adhesion and activation of platelets, resulting in the release of pro-inflammatory and procoagulant mediators. The subsequent cascade of events includes the activation of plasma coagulation factors, which leads to the formation of a fibrin network stabilizing the thrombus [12]. Thrombogenesis contributes to the progression of atherosclerotic plaques, causing their destabilization, rupture, and the potential occurrence of acute cardiovascular events [13]. In this way, the thrombotic process constitutes an integral element linking inflammation, vascular damage, and the clinical manifestations of atherosclerosis.

In the development of atherosclerotic disease, increasing attention is being given to neurohormonal activation. Key mechanisms in this context involve the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system activation. Angiotensin II, the main effector of the RAAS, promotes vasoconstriction, oxidative stress, and inflammatory processes within the vascular wall, facilitating the formation and destabilization of atherosclerotic plaques [14]. Simultaneously, activation of the sympathetic nervous system leads to increased catecholamine levels, which intensify inflammatory responses, activate platelets, and stimulate smooth muscle cell proliferation within the arterial vessels [15]. These neurohormonal mechanisms not only contribute to endothelial damage but also promote thrombus formation, which can result in acute cardiovascular events such as myocardial infarction or stroke [16]. Thus, neurohormonal activation represents a critical factor integrating hemodynamic, inflammatory, and pro-thrombotic processes in atherosclerosis.

In recent years, many serum biomarkers related to the development and progression of atherosclerosis have been discovered [17]. The familiarization with these biomarkers has enabled the creation of predictive models for the early detection of atherosclerosis and its complications. In this section of the article, current biomarkers of the disease, as well as new potential ones for early disease identification, will be described.

2. Biomarkers

An ideal biomarker should be characterized by high sensitivity, specificity, reproducibility, and ease for clinical application. The most commonly used biomarkers in clinical practice for detecting atherosclerosis, such as LDLC, HDLC or TGs level in blood

serum, unfortunately are not useful for all patients, and their predictive value is limited to specific groups of the population with high or very high cardiovascular risk [18]. Therefore, scientists have discovered new, more specific molecules responsible for the development of atherosclerosis, correlated with various stages of the atherosclerosis development - inflammatory process, destabilization of the atherosclerotic plaque, thrombocyte activation, neurohormonal activation, shear stress in the vascular endothelium [19].

2.1. Lipoproteins

2.1.1. Currently identified lipoprotein biomarkers

One of the first stages in the pathogenesis of atherosclerosis is the deposition of various plasma lipoproteins in the subendothelial arterial space, particularly at sites where blood flow has been impaired. A strong correlation has been demonstrated between high levels of LDLC and susceptibility to cardiovascular diseases. The same lipoprotein is the primary source of lipids that accumulate within the cells of arterial walls [20]. On the other hand, high levels HDLC has an opposite effect, hindering the development of foam cells by facilitating the process of lipid removal from the arterial wall cells [21]. Based on density, size, and differences in the physical and chemical parameters two main phenotypes of LDL particles can be identified: phenotype A, characterized by a high content of large buoyant LDL (lbLDL), and phenotype B, where small dense LDL (sdLDL) predominates. There is also an intermediate form – phenotype A/B [22]. According to recent studies, a clear correlation with both ischemic heart disease and metabolic disorders such as obesity [23] and type 2 diabetes [10 24] is attributed to phenotype B. It is also a cause of reduced protective HDL levels and elevated triglyceride levels [25]. Due to the small size of sdLDL, it easily penetrates the walls of arteries, where it contributes to the formation and storage of atherosclerotic plaques. The predominance of sdLDL is recognized as a risk factor for cardiovascular diseases (CVD) according to the National Cholesterol Education Program (NCEPIII) [26].

It is also important to highlight the role of lipoprotein(a) [Lp(a)] as an additional risk factor for cardiovascular events. This molecule is structurally alike LDL – it contains apolipoprotein B100 (apo B100) in its structure and has a similar size and lipid composition. One of the main differences between LDL and Lp(a) is the presence of an additional protein-apolipoprotein (a) [apo (a)]. Many scientists have shown a link between Lp(a) and

inflammatory cytokines such as IL-6, tumor necrosis factor-alpha (TNF-α), and transforming growth factor-beta (TGF-β), confirming the pro-inflammatory effect of Lp(a) on the arterial wall [27]. Additionally, the homology between Lp(a) and plasminogen has been proven. This discovery led to the hypothesis of a mechanism linking thrombogenesis and atherosclerosis with plasma lipoproteins – by competing with plasminogen for binding sites on endothelial cells, Lp(a) inhibits fibrinolysis and initiates the process of intravascular thrombosis [28].

2.1.2 Potential future biomarkers of lipoproteins

Oxidized low-density lipoprotein (oxLDL**)** is currently considered as a significant biomarker useful in assessing the risk of atherosclerosis. Studies show that elevated levels of oxLDL in the blood correlate with the presence of atherosclerotic lesions, which allows this indicator to be used in cardiovascular risk assessment [29]. Within the intima, reactive oxygen species (ROS) initiate the oxidation of low-density lipoproteins, while also facilitating the uptake of oxLDL by macrophages. The formation of oxLDL activates vascular endothelial cells, leading to increased expression of adhesion molecules, such as vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 ICAM-1, which assist in the migration of monocytes into the arterials inner layer. Consequently, these molecules participate in attracting monocytes, T-lymphocytes, and mast cells to the vessel's inner wall. OxLDL also stimulates macrophages, which engulf these particles through so-called scavenger receptors, such as CD36 and Lectin-like Oxidized Low-Density Lipoprotein Receptor-1 (LOX-1). This process promotes the formation of foam cells, a key component of atherosclerotic plaque. With the accumulation of foam cells and lipids, the plaque becomes unstable, potentially leading to thrombus formation and acute cardiovascular events [30].

Several studies indicate that elevated oxLDL levels are more frequently observed in patients with risk factors such as hypertension, diabetes, smoking, and obesity [31]. Additionally, research on oxLDL demonstrates its prognostic value—patients with elevated oxLDL levels have a higher risk for developing coronary artery disease, myocardial infarction (MI) and other vascular complications [32]. The application of oxLDL as an atherosclerosis marker may have significant clinical relevance. Monitoring oxLDL levels can assist physicians in identifying patients at high risk of developing atherosclerosis and its complications, as well as in tracking the effectiveness of therapies, such as statin use. In the human study conducted by Gjin Ndrepepa et al. on humans, the effectiveness of statin therapy in reducing oxLDL levels was proven ($P = 0.0001$) [33].

2.2 Currently identified biomarkers of inflammation

2.2.1. C-reactive protein (CRP)

C-reactive protein (CRP) is a highly sensitive but non-specific marker of inflammatory conditions. It is primarily synthesized in hepatocytes in response to stimulation by various inflammatory mediators, including IL-6, IL-1, and TNFs. The preferred method for measuring CRP in blood, recommended by the Food and Drug Administration (FDA), is the high sensitivity method (hsCRP) [34].

There are reports of extracellular production of CRP by cells located near atherosclerotic plaques. Therefore, elevated CRP levels may also indicate plaque destabilization and can be used for early detection of atherosclerosis [35]. The literature suggests that CRP influences on the regulation of adhesion molecules, facilitates the uptake of LDL by macrophages, increases the release of monocyte chemoattractant protein-1 **(**MCP-1), and inhibits nitric oxide production—all of which are crucial processes in the pathogenesis of atherosclerotic plaque formation [36]. Several large prospective studies, including the Physicians' Health Study and the Women's Health Study, have shown that even a small increase in CRP levels in potentially healthy individuals is associated with approximately a two-fold increase in the risk of MI in the future [37,38].

2.2.2. Uric acid (UA)

Uric acid (UA) is the end-stage product of purine metabolism in humans. Numerous studies have been conducted to assess the independent positive impact of uric acid (UA) on cardiovascular mortality. Some of these confirm the association between elevated UA levels and the development of cardiovascular disease (CVD) through mechanisms such as increasing oxidative stress or promoting endothelial dysfunction [39]. Nevertheless, there is considerable evidence suggesting that hyperuricemia is not necessarily a risk factor for CVD, but rather a consequence of it [40]. Further research is needed to definitively determine the role of uric acid in the pathogenesis of vascular diseases and its utility as a biomarker for early detection of atherosclerosis.

2.3 Potential future biomarkers of inflammation

2.3.1 Interleukin 6

IL-6 is one of the main pro-inflammatory cytokines released by endothelial cells, macrophages, monocytes, and other inflammatory cells in response to risk factors for atherosclerosis, such as elevated LDL levels, smoking, obesity, and chronic stress. IL-6 acts on immune system cells, stimulating them to release other cytokines and chemokines that exacerbate the inflammatory response in the walls of arteries [41, 42]. Furthermore, IL-6 stimulates the expression of adhesion molecules on the surface of endothelial cells, such as VCAM-1 and ICAM-1. Both of them facilitate the attraction and attachment of leukocytes (mainly monocytes and lymphocytes) to the vessel wall, which is a crucial step in the formation of atherosclerotic plaques [43]. An important aspect linking atherosclerosis development with IL-6 is its impact on lipid metabolism. By increasing TGs levels and altering lipoprotein function, IL-6 can lead to excessive lipid accumulation in the walls of blood vessels. IL-6 can also affect LDL and HDL levels, raising LDL and lowering HDL, which promotes the development of atherosclerosis [44]. As a result of the chronic inflammation caused by IL-6, the risk of atherosclerotic complications, such as heart attack, stroke, or coronary artery disease, increases. IL-6 influences coagulation processes and may contribute to an increase in thrombin and fibrinogen activity, which are crucial for the formation of blood clots in narrowed arteries [45]. For this reason, IL-6 is considered a potential biomarker for early detection of atherosclerosis as well as a therapeutic target.

2.3.2 Myeloperoxidase (MPO)

Myeloperoxidase (MPO) is an enzyme from the peroxidase family that contains heme. It is primarily produced by polymorphonuclear neutrophils and macrophages [46]. Elevated MPO levels is one of the best markers of inflammation and oxidative stress, making this protein a sensitive but non-specific biomarker in many commonly occurring diseases, including atherosclerosis. MPO also plays a role in antibacterial and antiviral defense through the production of hypochlorous acid (HOCl) [47].

MPO not only participates in the inflammatory process but also mediates the destabilization of atherosclerotic plaques by contributing to the oxidation of LDL lipoproteins. Oxidized LDL is a highly atherogenic molecule [48]. It has been shown that higher MPO

levels are found in patients with ischemic heart disease and those who have had a MI compared to healthy individuals.

2.3.3 Growth-differentiation factor-15 (GDF-15)

Growth-differentiation factor-15 **(**GDF-15) is a protein that belongs to the TGF-β family. It has cytokine properties and it is primarily produced in response to various cellular stresses and inflammatory conditions [49]. In the context of atherosclerosis, GDF-15 plays an increasingly recognized role in the pathogenesis of the disease, influencing several key processes related to the development of atherosclerotic lesions and its complications such as stroke, peripheral artery disease, and even cardiovascular-related deaths[50].

The RELAX-AHF study revealed an interesting correlation between elevated GDF-15 levels in patients with acute heart failure, who were found to have a higher likelihood of adverse outcomes (P = 0,027) [51]. A GDF-15 value below 1200 ng/L indicated low cardiovascular risk and was considered the upper cut-off point for healthy individuals, whereas in the population of patients with non-ST-segment elevation acute coronary syndromes (NSTEMI), an optimal GDF-15 value for assessing cardiovascular risk was 1800 ng/L [52].

2.3.4 Fibrinogen

Fibrinogen is an acute-phase protein synthesized in the liver. It also plays a pivotal role in thrombus formation by participating in platelet aggregation, endothelial injury, and plasma viscosity [53]. Fibrinogen consists of three polypeptide chains: Aα, Bβ, and γ. A recent prospective study revealed a link between high levels of γ-fibrinogen and atherosclerosis and its complications, such as stroke, peripheral artery disease, and even cardiovascular-related deaths [54]. The literature has shown higher levels of fibrinogen in patients with an elevated risk of cardiovascular disease (CVD) incidents compared to healthy individuals. In a large FSC study that analyzed 31 prospective studies, the relationship between fibrinogen levels and the risk of both major vascular and non-vascular outcomes was assessed in patients without known CVD. The results of this study demonstrated that fibrinogen levels were a risk factor for stroke, coronary artery disease (CAD), and mortality [55]. Above paragraphs suggest fibrinogen could become a new marker for assessing cardiovascular risk.

2.4 Other potential biomarkers of atherosclerosis

2.4.1 microRNA (miRNA)

MicroRNA (MiRNAs) is a group of molecules consisting of 21-23 nucleotides in length that play a crucial role in regulating gene expression [56]. In the last decade, there has been a growing interest in miRNA in the context of atherosclerosis pathophysiology. Numerous scientific studies have demonstrated that miRNA plays a pivotal role in maintaining cardiovascular homeostasis [57]. Alterations in miRNA expression levels are associated with the pathogenesis of plaque formation and progression in atherosclerosis. miRNA primarily regulates translation at the post-expression level and can prevent gene expression, typically through two mechanisms: translational repression and mRNA degradation.

The early stages of atherosclerosis development include endothelial dysfunction, inflammatory responses, and foam cell formation. There is an extensive list of miRNAs that regulate endothelial function, such as miR-221, miR-503, miR-217, miR-34a, miR-181b, miR-155, miR-126, miR-1, miR-223, miR-145, miR-146a, miR-92a, and miR-10a [58].

MiRNA-126, one of the most extensively studied microRNAs, reduces VCAM-1 expression induced by tumor necrosis factor-alpha (TNF-α), leading to increased vascular permeability and the expression of adhesion molecules, thereby facilitating the migration of white blood cells into the vessel wall [59]. This process adversely affects blood vessels structure, promoting inflammation.

Furthermore, miR-155 contributes to the inflammatory mechanism in endothelial cells (EC) by downregulating vasodilatatory nitric oxide synthase (NOS), E26 transformation-specific sequence (ETS-1), and subsequent inflammatory molecules. MiR-155 also plays a critical role in the angiotensin II signaling pathway, significantly influencing processes such as cardiac remodeling, heart failure, and the progression of atherosclerosis [60].

Another crucial function of miRNAs is the regulation of both differentiation and proliferation of vascular smooth muscle cells (VSMCs). Overexpression of miR-21 has been identified as a promoter of vascular SMCs proliferation. Conversely, the inhibition of miR-221 and miR-222 acts as a negative regulator, reducing the rate of vascular SMCs proliferation by suppressing c-Kit, p27 (Kip1), and p57 (Kip2) [61].

Interestingly, some miRNAs, including miR-10a, miR-19a, miR-23b, miR-101, and miR-143/145, may have a protective role in the development of atherosclerosis [62, 63]. Their

atheroprotective effects may include reducing oxidative stress, which contributes to the formation of atherosclerotic plaques [64]. Additionally, they can modulate the expression of genes involved in inflammations and may suppress the activity of pro-inflammatory cytokines and chemokines, potentially preventing excessive inflammation in the vessel walls [65].

MicroRNAs play an extraordinarily significant role in the progression of atherosclerosis and, consequently, in the development of CAD. It is important to consider the bifunctional profile of these molecules, with some exhibiting pro-atherogenic effects, such as miR-122, miR-92a, and the miR-17-92 cluster, while others demonstrate atheroprotective properties, such as miR-30c, miR-148a, and miR-21 [66].

Additionally, this year's Nobel Prize in Physiology or Medicine in 2024 was awarded to Victor Ambros and Gary Ruvkun for the discovery of microRNA and its role in post-transcriptional gene regulation, highlighting the significant interest in these molecules and their potential applications in clinical practice.

2.4.2 Lipoprotein-associated phospholipase A2 (Lp-PLA2)

Lipoprotein-associated phospholipase A2 (Lp-PLA2), known as platelet-activating factor acetylhydrolase, belongs to the phospholipase A2 superfamily and is primarily produced by monocytes and macrophages. By participating in the hydrolysis of LDL particles, Lp-PLA2 contributes to the augmentation of their oxidative susceptibility. Subsequently, Lp-PLA2 is involved in the release of lysophosphatidylcholine and fatty acids oxidation, which trigger an inflammatory cascade. The accumulation of lysophosphatidylcholine and oxidized fatty acids contributes to the transformation of macrophages into foam cells, a key component in the formation of atherosclerotic plaques [67].

Elevated levels of Lp-PLA2 have been shown to be a significant determinant of CAD and ischemic stroke in populations without traditional risk factors [68]. On the other hand, several large randomized studies have not demonstrated benefits from using Lp-PLA2 inhibitors in patients with CAD [69]. As a result of these studies, the clinical utility of Lp-PLA2 as a biomarker for early detection of atherosclerosis remains unclear. Therefore, further research is needed to determine whether Lp-PLA2 plays a causal role in cardiovascular events.

2.4.3 Secretory phospholipase A2 (sPLA2)

Secretory phospholipase A2 (sPLA2) is an enzyme associated with lipid metabolism and plays a significant role in inflammatory processes, making it a potential biomarker for atherosclerosis. Studies have shown that higher sPLA2 levels correlate with an increased risk of cardiovascular events such as myocardial infarction, stroke, and sudden cardiac death [70]. However, there is evidence challenging the assumption that elevated sPLA2 levels is a crucial prognostic factor for CAD. In a clinical trial investigating the sPLA2 inhibitor varespladib, no benefits were observed in patients with acute coronary syndromes (ACSs). Moreover, the drug significantly increased the risk of myocardial infarction (MI) ($P = .04$)[71].

In conclusion, sPLA2 is a promising biomarker for atherosclerosis, but its clinical application requires further research. It could become an important tool in assessing cardiovascular risk, particularly in the context of targeted anti-inflammatory therapies.

2.4.4.Soluble CD40 ligand (sCD40L)

Soluble form of CD40 (sCD40L ligand) is a protein involved in the immune system and inflammatory processes, playing a significant role in the pathogenesis of atherosclerosis and cardiovascular diseases. CD40L, a membrane-bound molecule, undergoes proteolysis, leading to the formation of its soluble form (sCD40L), which is present in the bloodstream [72]. There is opposing evidence supporting the value of sCD40L as a biomarker for detecting cardiovascular risk and evidence challenging its usefulness. In the large study with acronym “Acute Nondisabling Cerebrovascular Events (CHANCE)” elevated levels of sCD40L were shown to correlate with recurrent stroke in patients with minor stroke and transient ischemic attack [73]. However, reports on the utility of sCD40L in patients with acute myocardial infarction (AMI) are inconclusive. Some researchers have even shown that sCD40L is not associated with mortality or myocardial infarction risk [74].

sCD40L is a promising biomarker for atherosclerosis because it reflects both inflammatory and thrombotic processes related to the pathogenesis of cardiovascular diseases. However, its application in clinical practice requires further studies to accurately determine its diagnostic and prognostic value and to optimize measurement methods.

2.4.5.Copeptin

Copeptin is a low-molecular-weight protein and a stable fragment of the precursor of vasopressin (antidiuretic hormone, ADH). The plasma half-life of copeptin is longer

compared to that of vasopressin [75]. For this reason, it is increasingly being studied as a potential biomarker in various clinical conditions, including cardiovascular diseases such as atherosclerosis. Copeptin is released in response to physiological stress, including hypoxia, hypovolemia, and endothelial damage, which are phenomena associated with atherosclerosis [76]. Recent studies have demonstrated a link between elevated copeptin levels and the progression of coronary artery disease (CAD), as well as an increased risk of mortality from cardiovascular incidents [77].

Copeptin holds potential as a biomarker for atherosclerosis because it reflects vasopressin activity and the physiological stress related to vascular damage. However, its routine clinical application requires further research, particularly to determine its specificity and sensitivity compared to other biomarkers.

2.4.6.Mid-Regional Pro-Adrenomedullin (MR-proADM)

Mid-Regional Pro-Adrenomedullin (MR-proADM) is a stable fragment of the precursor of adrenomedullin (ADM), a peptide hormone with vasodilatory, anti-inflammatory, and antimicrobial properties. Due to its stability in plasma and reliable measurement capabilities, MR-proADM is emerging as a biomarker for various clinical conditions, particularly in cardiovascular, infectious, and inflammatory diseases. Recent studies have demonstrated that elevated levels of MR-proADM have strong prognostic value for mortality and morbidity in patients with heart failure following acute myocardial infarction. It is suggested that MR-proADM may outperform N-terminal pro-B-type natriuretic peptide (NT-proBNP) in assessing the risk of death due to CVD [78].

MR-proADM is a promising biomarker in clinical practice, particularly for cardiovascular diseases, sepsis, and respiratory conditions. Its ability to provide insights into disease severity and prognosis makes it a valuable tool for early diagnosis and therapeutic monitoring, though further research is needed to establish its full clinical utility.

3. Conclusion

Advances in the identification of new markers of atherosclerosis open up new perspectives in the diagnosis, prognosis, and monitoring of this chronic disease. Their ability to reflect biological processes such as physiological stress, endothelial dysfunction, and inflammation and thrombotic complications can significantly complement traditional markers, such as LDL cholesterol or C-reactive protein.

Although initial studies have shown promising results, the routine application of these biomarkers in clinical practice requires further, large-scale research. It is crucial to establish the specificity and sensitivity of these markers, their role in risk assessment, and the benefits of integrating them into diagnostic and therapeutic algorithms.

In the future, the implementation of these modern markers may contribute to more precise risk assessment, better monitoring of disease progression, and personalized therapy, ultimately improving the prognosis for patients with atherosclerosis.

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