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Risk Factors for Early Vascular Ageing: A Review of Current Evidence

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Abstract

Early vascular ageing (EVA) has become an increasingly important concept in cardiovascular medicine, representing a state in which structural and functional changes of the arterial system occur at a younger age than expected. Unlike chronological ageing, which follows a predictable biological course, EVA reflects an acceleration of vascular decline that predisposes individuals to premature cardiovascular events, stroke, and increased mortality. The central hallmarks of EVA include arterial stiffening, endothelial dysfunction, intima-media thickening, and extracellular matrix remodeling. These alterations are strongly linked to both traditional and emerging cardiovascular risk factors.

This review aims to provide a comprehensive synthesis of current evidence regarding the major determinants of EVA. A structured search of PubMed, Scopus, and Web of Science databases identified epidemiological, clinical, and mechanistic studies published between 2000 and 2024. The findings indicate that non-modifiable risk factors such as age, sex, and genetic predisposition establish the baseline susceptibility to vascular ageing, but modifiable factors play the dominant role in determining the speed and severity of progression. Hypertension, diabetes mellitus, obesity, dyslipidemia, and smoking consistently emerge as the strongest drivers of EVA. Lifestyle-related influences, including sedentary behavior, poor dietary habits, and chronic psychosocial stress, also play significant roles. Moreover, novel contributors such as exposure to environmental pollutants and gut microbiota dysbiosis have been increasingly implicated, expanding the scope of EVA research beyond traditional cardiovascular medicine.

Importantly, the evidence demonstrates that EVA is not irreversible. Lifestyle modification, including regular physical activity, adherence to cardioprotective diets, and smoking cessation, improves arterial elasticity and endothelial function. Pharmacological interventions such as antihypertensive, lipid-lowering, and antidiabetic agents have also been shown to mitigate or delay the onset of EVA. Novel therapeutic approaches targeting oxidative stress, chronic inflammation, and endothelial repair are currently under investigation and may further enhance prevention.

In conclusion, EVA should be recognized as a clinically relevant and potentially preventable condition. Early identification of individuals at risk, integration of vascular ageing markers such as pulse wave velocity into cardiovascular risk assessment, and timely implementation of preventive strategies are essential to reduce the burden of premature cardiovascular disease. By reframing vascular ageing as a modifiable rather than an inevitable process, healthcare systems can shift focus from late-stage treatment to proactive prevention, ultimately improving population health and longevity.

Keywords: *early vascular ageing, arterial stiffness, endothelial dysfunction, cardiovascular risk, lifestyle modification.*

INTRODUCTION

Vascular ageing is an inevitable biological process that progressively affects the structure and function of the arterial system. In healthy ageing, these changes occur gradually and are often not clinically evident until later decades of life. They include increased arterial stiffness, loss of vascular compliance, thickening of the intima-media layer, and impaired endothelial function [1]. However, in a subset of individuals,

these alterations occur much earlier than expected for their chronological age, giving rise to a condition now widely referred to as early vascular ageing (EVA). EVA represents a state of accelerated vascular decline that predisposes affected individuals to premature cardiovascular disease, stroke, and increased overall mortality [2], [3].

The concept of EVA has gained increasing recognition in recent decades as research has shifted from viewing vascular ageing as an inevitable consequence of chronological time to understanding it as a modifiable and preventable process. Arterial stiffness, measured non-invasively through pulse wave velocity (PWV) and augmentation index, has become a widely accepted biomarker of vascular ageing [4]. Endothelial dysfunction, reflected by reduced nitric oxide availability, increased oxidative stress, and heightened inflammatory activation, is another key marker of EVA [5]. Together, these changes compromise vascular homeostasis and accelerate the development of hypertension, atherosclerosis, and heart failure, highlighting the clinical relevance of identifying EVA in its earliest stages.

Global epidemiological data underscore the urgent need to address EVA. Cardiovascular disease remains the leading cause of death worldwide, responsible for nearly 18 million deaths annually [6]. Importantly, an increasing number of cardiovascular events are being observed in younger populations, suggesting that EVA contributes significantly to the global burden of premature morbidity. Longitudinal cohort studies have confirmed that individuals with elevated arterial stiffness and impaired endothelial function at a young age face higher risks of cardiovascular disease and all-cause mortality later in life [7]. Thus, EVA is not merely an academic concept but a clinically significant predictor of early disease burden.

Multiple studies have attempted to delineate the risk factors that accelerate vascular ageing. Traditional cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, smoking, and obesity remain central to the pathogenesis of EVA [8], [9]. Hypertension in particular exerts chronic mechanical stress on the arterial wall, leading to elastin fragmentation and collagen accumulation, thereby promoting arterial stiffening [10]. Diabetes and insulin resistance accelerate vascular ageing through hyperglycemia-induced oxidative stress and advanced glycation end-product accumulation, which impair endothelial function [11]. Similarly, obesity and metabolic syndrome contribute to EVA by driving systemic inflammation and metabolic dysregulation [12].

Beyond these classical determinants, modern research has highlighted a range of emerging factors that further contribute to EVA. Physical inactivity and sedentary lifestyle are strongly associated with impaired arterial elasticity, while regular exercise has been shown to restore vascular compliance [13]. Dietary factors, particularly high salt intake and low consumption of fruits and vegetables, play a crucial role in modulating vascular health [14]. Psychosocial stress and depression have also been linked to EVA, mediated by dysregulation of the hypothalamic-pituitary-adrenal axis and systemic inflammation [15]. Environmental exposures, including long-term air pollution, are increasingly recognized as contributors to vascular dysfunction [16]. More recently, the gut microbiota has been implicated in the regulation of vascular ageing, with alterations in microbial composition and metabolites influencing vascular inflammation and tone [17].

Importantly, EVA is not uniform across populations but is shaped by genetic and epigenetic factors. Genetic predisposition influences susceptibility to arterial stiffening, while epigenetic modifications induced by environmental exposures and lifestyle behaviors may alter vascular ageing trajectories across generations [18]. Sex also plays a modifying role, with women demonstrating relative protection against EVA during reproductive years due to estrogen's vasoprotective effects, though this advantage diminishes post-menopause [19].

Taken together, these findings suggest that EVA is a complex, multifactorial condition shaped by both intrinsic and extrinsic factors. Unlike chronological ageing, EVA represents an accelerated and potentially reversible process. Identifying its determinants provides opportunities for early detection, prevention, and intervention. The purpose of this review is therefore to synthesize current evidence on the risk factors associated with EVA, highlighting both well-established and emerging contributors. By clarifying the pathways through which these risk factors accelerate vascular ageing, the review aims to support more effective preventive strategies and clinical interventions to reduce the global burden of premature cardiovascular disease.

METHODS

The analysis of the available literature demonstrates that early vascular ageing (EVA) is not a uniform phenomenon but rather the outcome of a multifactorial interplay between genetic predisposition,

environmental exposures, and lifestyle-related determinants. The reviewed studies consistently showed that non-modifiable risk factors such as chronological age, sex, and hereditary background provide the foundation upon which vascular changes evolve, yet the speed and severity of these changes are largely shaped by modifiable influences.

Chronological age remains the most important baseline determinant of vascular ageing. Across all cohorts, advancing age was associated with progressive arterial stiffening, increased pulse wave velocity, and endothelial dysfunction. However, studies consistently reported that individuals with EVA exhibit these changes much earlier than expected for their age group. For example, large population-based studies demonstrated that young adults with uncontrolled hypertension or obesity displayed arterial stiffness profiles comparable to individuals a decade older, confirming that EVA reflects accelerated biological ageing of the vasculature rather than chronological progression alone [1], [2].

Genetic predisposition also emerged as a strong non-modifiable factor. Several polymorphisms influencing nitric oxide synthase activity, collagen deposition, and inflammatory cytokine regulation were associated with higher susceptibility to EVA. Family history of premature cardiovascular disease was consistently linked to increased vascular stiffness in offspring, even in the absence of overt risk factors, suggesting a heritable component [3]. Sex differences were also prominent. Premenopausal women generally demonstrated delayed onset of EVA compared with men of the same age, a protection attributed to the vasodilatory and anti-inflammatory properties of estrogens. However, postmenopausal women exhibited rapid progression of vascular ageing, ultimately narrowing the sex gap [4].

Among the modifiable risk factors, hypertension was the most consistently reported determinant. Studies employing pulse wave velocity measurements confirmed that individuals with chronic elevated blood pressure exhibited significantly greater arterial stiffness than normotensive counterparts, independent of age. Longitudinal data further established hypertension as both a cause and consequence of arterial stiffening, creating a self-perpetuating cycle of vascular deterioration [5]. Diabetes mellitus and insulin resistance were equally significant. Patients with type 2 diabetes exhibited increased arterial stiffness and impaired endothelial-dependent vasodilation, with the severity of glycemic control strongly influencing outcomes. Hyperglycemia-induced oxidative stress and the accumulation of advanced glycation end products were frequently cited mechanisms linking diabetes to EVA [6].

Obesity and metabolic syndrome also showed a clear association with EVA. Excess adiposity was linked with chronic low-grade systemic inflammation, dysregulated adipokine secretion, and increased oxidative stress, all of which contribute to vascular remodeling. In studies involving children and adolescents, overweight individuals already displayed markers of EVA, indicating that obesity accelerates vascular ageing from an early age [7]. Dyslipidemia was another major contributor. Elevated LDL cholesterol and reduced HDL cholesterol levels were consistently associated with higher arterial stiffness and impaired endothelial function. Interventional trials showed that lipid-lowering therapies, particularly statins, improved vascular elasticity, supporting the causal role of dyslipidemia in EVA [8].

Cigarette smoking emerged as a potent accelerant of EVA. Both active smoking and passive exposure were associated with reduced nitric oxide bioavailability, endothelial injury, and increased arterial stiffness. Even low levels of smoking demonstrated measurable effects on vascular ageing, while cessation was associated with partial reversibility of arterial changes over time [9]. Physical inactivity and sedentary lifestyle were also repeatedly confirmed as independent risk factors. Individuals with low levels of physical activity exhibited significantly higher arterial stiffness, whereas regular aerobic exercise improved endothelial function, reduced oxidative stress, and increased arterial compliance [10]. Nutritional studies revealed that diets high in saturated fats, refined carbohydrates, and salt were strongly correlated with EVA, whereas adherence to Mediterranean dietary patterns was protective. Populations consuming diets rich in fruits, vegetables, whole grains, and omega-3 fatty acids consistently demonstrated lower measures of arterial stiffness [11].

Emerging evidence also highlighted novel contributors to EVA. Chronic psychosocial stress, including work-related stress and depression, was associated with higher pulse wave velocity and impaired endothelial function, independent of traditional risk factors. Studies investigating stress biomarkers such as cortisol demonstrated strong correlations with vascular ageing indices, suggesting that neuroendocrine dysregulation accelerates vascular decline [12]. Environmental exposures such as air pollution, particularly fine particulate matter, were consistently linked with increased arterial stiffness and higher risk of premature cardiovascular disease. Longitudinal studies conducted in urban populations revealed that long-term exposure to traffic-related pollutants accelerated vascular ageing even in otherwise healthy

individuals [13]. In recent years, gut microbiota has also been recognized as a potential determinant. Dysbiosis was shown to reduce production of beneficial metabolites such as short-chain fatty acids, increase systemic inflammation, and impair vascular function, thereby contributing to EVA [14].

Across the reviewed studies, a recurring theme was the additive and synergistic effect of risk factors. Individuals with multiple coexisting risk factors—such as obesity combined with hypertension and smoking—demonstrated the most pronounced vascular ageing, with arterial stiffness values far exceeding those explained by any single risk factor alone. This observation reinforces the importance of a holistic approach to prevention and management.

In summary, the results of this review demonstrate that EVA is a complex condition resulting from an interplay of both unavoidable and preventable factors. Non-modifiable determinants such as age, sex, and genetics set the biological baseline, but modifiable exposures including hypertension, diabetes, obesity, dyslipidemia, smoking, sedentary lifestyle, poor diet, stress, environmental pollution, and gut dysbiosis exert the greatest influence on the trajectory of vascular health. The weight of evidence underscores the critical importance of early detection and modification of these risk factors to prevent premature vascular decline and reduce the burden of early-onset cardiovascular disease.

RESULTS

The evidence consistently identifies EVA as the outcome of both genetic susceptibility and environmental or lifestyle exposures.

Non-modifiable risk factors include chronological age, sex, and hereditary background. Genetic polymorphisms affecting collagen synthesis, nitric oxide signaling, and inflammatory pathways have been shown to predispose to arterial stiffening [5]. Men generally exhibit earlier vascular ageing than women, although post-menopausal hormonal decline narrows this sex difference [6].

Modifiable risk factors play a dominant role in EVA. Hypertension is among the strongest determinants, as persistent elevated blood pressure accelerates elastin degradation and collagen deposition within arterial walls, thereby increasing pulse wave velocity [7]. Diabetes mellitus and insulin resistance contribute through hyperglycemia-induced oxidative stress and accumulation of advanced glycation end products, which impair endothelial function [8]. Obesity and metabolic syndrome exacerbate vascular ageing by promoting systemic inflammation, dyslipidemia, and insulin resistance [9]. Dyslipidemia, particularly elevated LDL cholesterol, contributes to vascular stiffening and atherosclerotic changes [10]. Cigarette smoking directly damages endothelial cells and reduces nitric oxide bioavailability, accelerating stiffening [11].

Table 1. Main risk factors associated with early vascular ageing and their mechanisms

Risk factor	Mechanism leading to EVA	Evidence strength
Hypertension	Elastin degradation, collagen deposition, arterial stiffening	Strong
Diabetes mellitus	Oxidative stress, advanced glycation end-products, endothelial dysfunction	Strong
Obesity & Metabolic syndrome	Systemic inflammation, adipokine imbalance, dyslipidemia	Strong
Smoking	Endothelial injury, nitric oxide reduction, oxidative stress	Strong
Sedentary lifestyle	Reduced vascular compliance, impaired nitric oxide signaling	Moderate
Unhealthy diet	High salt & fat intake, oxidative stress, inflammation	Moderate
Psychosocial stress	Neuroendocrine dysregulation, systemic inflammation	Emerging
Air pollution	Oxidative stress, vascular inflammation	Emerging
Gut microbiota	Reduced short-chain fatty acids, increased endotoxins	Emerging

Lifestyle factors have also been strongly linked to EVA. Physical inactivity is associated with impaired arterial compliance, whereas regular aerobic exercise enhances vascular elasticity and endothelial function [12]. Dietary patterns influence vascular ageing, with excessive salt, saturated fats, and processed foods accelerating EVA, while Mediterranean-style diets rich in fruits, vegetables, and unsaturated fats exert protective effects [13].

Emerging contributors include psychosocial stress, environmental pollution, and gut microbiota. Chronic psychological stress has been associated with dysregulation of the hypothalamic-pituitary-adrenal axis and systemic inflammation, which accelerate arterial ageing [14]. Long-term exposure to fine particulate matter in air pollution independently predicts increased arterial stiffness [15]. Alterations in gut microbiota composition, with reduced production of beneficial metabolites such as short-chain fatty acids, have been linked to impaired vascular function [16].

DISCUSSION

The evidence demonstrates that EVA is a multifactorial condition resulting from both modifiable and non-modifiable determinants. Hypertension remains the most robust predictor of EVA, but diabetes, obesity, smoking, and poor diet contribute significantly and often synergistically. Clinical trials confirm that antihypertensive agents, statins, and antidiabetic therapies improve markers of arterial stiffness, supporting the causal role of these factors [7], [8], [10]. Lifestyle interventions, particularly regular exercise and dietary modification, remain the cornerstone of prevention. For instance, adherence to the Mediterranean diet has been shown to reduce arterial stiffness and improve endothelial function in both healthy individuals and patients with cardiovascular risk factors [13].

Emerging evidence highlights the role of novel determinants. Psychosocial stress and depression exert measurable effects on vascular ageing independent of traditional risk factors [14]. Air pollution is increasingly recognized as a global driver of cardiovascular risk through its impact on oxidative stress and vascular inflammation [15]. The gut microbiota represents a rapidly expanding field, with accumulating data suggesting its influence on systemic inflammation and vascular tone [16].

The clinical implications of these findings are significant. Assessment of vascular age using non-invasive measures such as pulse wave velocity can improve cardiovascular risk stratification beyond traditional models. Incorporating EVA screening into clinical practice would allow for earlier identification of at-risk individuals and timely interventions. Preventive strategies that combine lifestyle modification with pharmacological treatment hold promise for delaying or reversing premature vascular ageing.

CONCLUSION

The phenomenon of early vascular ageing (EVA) represents an increasingly recognized determinant of premature cardiovascular morbidity and mortality. While vascular ageing is a universal and unavoidable biological process, its acceleration in the form of EVA underscores the importance of distinguishing between chronological and biological ageing of the vascular system. This review has synthesized the current evidence and demonstrated that EVA results from a complex interplay between non-modifiable factors such as genetics, sex, and age, and a wide range of modifiable determinants, including hypertension, diabetes, dyslipidemia, obesity, smoking, sedentary lifestyle, poor dietary patterns, psychosocial stress, environmental pollution, and gut microbiota alterations. The cumulative effect of these influences determines the trajectory of vascular health and explains the heterogeneity observed among individuals of similar chronological age.

The strongest evidence implicates hypertension, diabetes, obesity, and smoking as dominant drivers of EVA, with large-scale cohort studies confirming their direct association with arterial stiffness and endothelial dysfunction. Importantly, emerging data emphasize the role of less traditional but equally impactful risk factors, including psychosocial stress and exposure to air pollution, which may act independently or synergistically with classical determinants. The growing interest in gut microbiota further highlights that EVA is not confined to vascular biology alone but is integrated within systemic metabolic and immunological pathways.

A key implication of the evidence is that EVA is not an irreversible fate. Lifestyle interventions such as increased physical activity, smoking cessation, weight management, and adoption of cardioprotective dietary patterns consistently demonstrate measurable improvements in arterial compliance and endothelial function. Pharmacological interventions, including antihypertensives, lipid-lowering agents, and antidiabetic therapies, have also shown efficacy in slowing the progression of vascular stiffening.

Moreover, novel therapeutic approaches targeting oxidative stress, inflammation, and endothelial repair represent promising future strategies. These findings collectively reinforce the paradigm that EVA is a preventable and modifiable condition when recognized early and addressed proactively.

Another critical point is the need for clinical integration of EVA assessment into cardiovascular risk stratification. Conventional risk calculators based solely on chronological age, cholesterol levels, and blood pressure may underestimate the true vascular risk of younger individuals with EVA. The incorporation of vascular ageing markers, such as pulse wave velocity and augmentation index, into clinical practice would allow earlier identification of individuals at risk and enable timely intervention before irreversible structural damage occurs. Such a shift towards biological rather than chronological assessment of vascular health could significantly improve preventive cardiology and reduce the burden of premature cardiovascular disease worldwide.

Despite substantial progress, important gaps remain in our understanding of EVA. There is still a need to establish standardized diagnostic criteria, to validate novel biomarkers, and to clarify the precise contribution of emerging determinants such as environmental exposures and gut microbiota. Longitudinal studies that integrate molecular, clinical, and lifestyle data will be essential for unraveling the complex mechanisms underlying EVA. Furthermore, research should prioritize diverse populations to account for differences across ethnic, socioeconomic, and geographical groups.

In conclusion, EVA should be viewed not simply as an academic construct but as a critical clinical and public health issue. Its recognition highlights that vascular ageing is not solely determined by time but is strongly shaped by modifiable exposures. The evidence reviewed here provides a strong rationale for early detection, aggressive management of cardiovascular risk factors, and promotion of healthy lifestyle behaviors to delay or reverse premature vascular decline. By shifting the focus from treatment of established cardiovascular disease to prevention of vascular ageing, we may achieve significant reductions in morbidity, mortality, and healthcare burden. The challenge for future research and clinical practice will be to translate these insights into effective strategies that safeguard vascular health across the lifespan.

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