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Exploring the Interconnections between Diabetes, Hypertension, Heart Diseases, and the Vascular System

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Abstract:

The complex interconnections among diabetes, hypertension, heart diseases, and the vascular system are perplexing to unscramble and challenging to figure out preventive and management strategies. The trail between these four diseases is so closely interwoven. First, in the onset and progression of lifestyle-related vascular diseases, including diabetes and hypertension, the vascular system plays a crucial role and is combined with metabolic and micro-vascular systems within the affected body. Second, diabetes and hypertension are their own independent risk factors for increasing the abnormal structure and function of the large arteries, heart, kidney, and other peripheral organs. The development of diabetes and hypertension-related heart diseases is essentially in the vascular system, but the existence of extra-cardiac and/or intrinsic heart diseases can noticeably influence the heart's performance and drastically render risk to less noticed, specific kinds of heart diseases. Third, the development of each type of arterial stiffness due to diabetes, hypertension, and other reasons is dissimilar, and in the same person, combined effects displayed more damaging results. However, it is also a life to be designed meticulously in order to fine-tune with the upper limits of the multiplicity of lifestyle-related risks so as to obtain the composite effects from these vantage points of onset and progression of these diseases and better learn how one can tailor the composite lifestyle-related preventive measures and management strategies. Fundamental advancement in vascular biology and understanding the roles of smoothed muscle cells, endothelium, and extracellular materials in relation to metabolism involving lipids, proteins, and each individually and holistically of the large and microvascular systems are prerequisites. Further, diabetes, hypertension, and heart and their related large arteries and landscapes are to be explored more thoroughly concerning abnormal structure, function, and related atherosclerosis, arteriosclerosis, and fibrosis.



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INTRODUCTION

Worldwide, diabetes and hypertension are growing at an alarming rate (Ababneh *et al.*, 2024). Hypertension remains a consistent economic and healthcare problem for middle, low-income, and high-income countries (Zhou *et al.*, 2021). Heart diseases occupy the foremost position among male and female patients above 40 years (Iqbal *et al.*, 2018; Rodgers *et al.*, 2019). And it's a severe disorder, which caused the most deaths throughout the world, with coronary heart disease and stroke being the main underlying reasons (Bani-Salameh *et al.*, 2021; Irfan *et al.*, 2019; Martin *et al.*, 2024).

In understanding diabetes and chronic diseases, the most important system is the vascular system (Li *et al.*, 2023). The fast development of cardio and cerebrovascular diseases in diabetic patients suggests the presence of an innate connection. In diabetic patients, hyperglycemia is a significant factor responsible for the initiation and evolution of diabetic micro and macrovascular complications (Ortega *et al.*, 2021). Based on different epidemiological, clinical, and therapeutic grounds, diabetic macro and microangiopathy share similar pathophysiological mechanisms (Alkhatib, 2019; Maida *et al.*, 2022).

Diabetes patients with chronic micro-thrombosis in small vessels and poor circulation already have the basis for the formation of macro-thrombosis, for instance in heart and cerebrovascular diseases, which are the main reason for the burst development of cardiovascular diseases and cerebrovascular diseases in diabetic patients (Alkhatib, 2021; Chang and Hawley, 2021). At the same time, various pathophysiological derangements that cause the formation of micro complications such as increased advanced glycosylation products, protein kinase c activation, the formation of hyperosmolar environment, oxidative stress, hyperlipemia, and slow blood flow, also exacerbate the macro blood vessel walls directly in different ways, such as endothelial

dysfunction, damage to large proteins etc. (Al-Refaai *et al.*, 2017; Tripathi and Mishra, 2023).

The disease duration and severity of diabetic microangiopathy are the most significant risk factors with multiple diabetic-associated risk factors determining the development of diabetes, myocardial infarction, cerebrovascular disease, and lower extremity arterial disease (Natorska, 2021). At the same time, it was shown that diabetes is an independent risk factor for vascular stenosis and directly correlates with the severity of vascular stenosis caused by atherosclerosis and that diabetes is not only an independent risk factor but aggravates the development of co-morbid diseases (Alkhatib, 2024; Zhang *et al.*, 2021). Furthermore, this micro-macro-vessel conjoined pathology also suggests identical or similar treatment strategies (Mourino-Alvarez *et al.*, 2021). Although it's not resolved just how microvascular disease leads to macrovascular disease, it is possible to see from these simple concepts that the formation and development of these conditions are inherently connected (Al-Khatib and Al-Alawneh, 2013; Roderburg *et al.*, 2021). These grounds involve the issue explored further in this essay (Baran *et al.*, 2021).

Understanding Diabetes and its Relationship with Hypertension

Diabetes is a prevalent global epidemic that is incited by an amalgamation of factors involving hereditary predisposition, dietary habits, lifestyle, and toxicants (Muhammad *et al.*, 2013; Wang *et al.*, 2021). Diabetes disrupts the body's equilibrium of blood sugar levels, either because of an absence of insulin (type 1 diabetes) or because cells resist insulin's efforts to direct glucose into biological pathways (type 2 diabetes) (Cheung and Li, 2012; Erekat *et al.*, 2014). Verily, type 2 diabetes is usually due to a mutation in insulin and after that turns into insulin resistance, in which blood sugar is higher than it should be. Moreover, diabetes and hypertension are bedfellows, and if the patient is infected with both conditions, it can gradually

become worse (Dell'Isola *et al.*, 2024). Remarkably, the similarity could be up to 50% in some situations, displaying an interface in both the prevalence and the pathogenesis (Jyotsna *et al.*, 2023; Livingston *et al.*, 2024).

As a dynamic disease, diabetes can lead to a cascade of severe conditions, such as heart attack, stroke, vision problems even blindness, kidney failure, poor blood flow (and chilblains or ulcers), uropoiesis injury, and meningitis (Sinha and Haque, 2022). Underlying the above is the vascular network disease, and about 50% of diabetics quit the future chances of developing heart diseases affected by scorching the vessels of the heart muscle (Al-Jarrah *et al.*, 2012; Korkmaz, 2021). Additionally, the vessel walls become thickened due to fat and sugar, which hampers the effective supply of blood to every organ in the human body (Zakir *et al.*, 2023). Last, but not least, is the brain, it can cause dementia or hemorrhagic stroke in severe cases (Mlynarska *et al.*, 2024). Obviously, a common vessel network is the organizing principle that controls the human autoimmune system. Thereby, the relationship ought not to be neglected (Lee and Park, 2023). After a cycle of five-year follow-ups, 19 patients of them have hypertension (Akanchi *et al.*, 2022). Since the distribution of the stress change in the blood vessel conforms to a power law, this might explain why the criticality in such kind of anatomy underlies the co-existing of hypertension and diabetes (Chen *et al.*, 2023). Of course, the stress at the contour of the vessel can be mediated by the blood flow and modulated by the dynamical output of the heart, which largely depends on its shape (Tohirova and Shernazarov, 2022). Except for those characteristic cases as an aperçu, it is valuable to glance at the epidemiology of the above two diseases from the worldwide to the individual aspects (Tan *et al.*, 2023).

Impact of Hypertension on Heart Diseases

People with hypertension have a higher risk of developing heart disease. Among all end-organ damage resulting from high blood pressure, heart diseases are the most common, perhaps

because the burden of high pressure is the greatest on the heart muscle (Egan and Schmouder, 1988). Chronic high blood pressure can lead to a variety of heart diseases (Reynolds *et al.*, 2022). Growing evidence shows that essential hypertension can induce changes in the structure, mass, and function of the left ventricle (Kim, 2021). The principal hemodynamic consequence of essential hypertension is increased left ventricular afterload, which stimulates the left ventricle to develop pressure overload, resulting in concentric left ventricular hypertrophy (Mitra *et al.*, 2021). The process also impairs the relaxation and compliance of the left ventricle and induces diastolic dysfunction (Dai *et al.*, 2021). All of these conditions will facilitate the occurrence of heart failure (Jones *et al.*, 2021). On the other hand, the risk of coronary artery disease is also increased with essential hypertension (Matsushita *et al.*, 2022).

The greater the severity of hypertension, as assessed by blood pressure level, duration, and burden, the greater the risk of experiencing myocardial infarction and clinical heart failure (Di Palo and Barone, 2022). Among subjects with essential hypertension, for any given level of blood pressure, the risk of heart failure increases with the presence of other coronary risk factors or the occurrence of LVH (Kaplon-Cieślicka *et al.*, 2022). The fact that both the left ventricle and the coronary vascular system are concomitantly affected by essential hypertension highlights the importance of endothelial function, which is impaired in both patients with essential hypertension and people with an increased risk of developing essential hypertension (Mitra *et al.*, 2021). It is an intermediary mechanism mediating the promotion of heart disease and heart failure by high blood pressure because essential hypertension gives rise to a series of pathogenic factors that ruin vascular health (Tadic *et al.*, 2021).

Vascular System: Linking Diabetes, Hypertension, and Heart Diseases

Diabetes, hypertension, and heart diseases often co-exist, interact through a variety of biological mechanisms, exacerbate each other,

and share common predisposing factors (Lourida and Louridas, 2022). The vascular system, a critical nexus connecting these conditions, has drawn increasing attention as a potential biological foundation for the interrelationship among these major chronic diseases (Ogunmuyiwa, 2023). Cardiovascular diseases including hypertension, coronary heart disease, and stroke are the most common causes of morbidity and mortality among diabetic patients. Type 2 diabetes significantly increases the risk of atherosclerosis in various arteries, including the coronary, carotid, and peripheral arteries, while mortality from atherosclerotic diseases accounts for as much as 80% of all fatalities in Type 2 diabetic patients (Zmaili *et al.*, 2024). The vascular system includes the circulatory system, which consists of the vessels in the blood and the lymph, and the lymphatic system that drains excess water from the body's organs (Bafei *et al.*, 2023). Atherosclerosis is recognized as the initiation and response to injury in the blood arteries and is, in fact, a systemic vascular disease, involving the initiation and progression of atherosclerosis in the blood vessels of all sizes in the body; it is not just a disease of big- or medium-sized blood vessels (Gundugurti *et al.*, 2022).

Diabetes and hypertension have been linked with endothelial dysfunction and increased vascular inflammation as key pathways to the early impairments in vascular integrity (Yang *et al.*, 2024). On the one hand, diabetes has been established to promote insulin resistance and vascular dysfunction, thereby compromising the vascular integrity of the endothelium-controlling vasodilation responses to various stimuli (Hildén *et al.*, 2023). On the other hand, hypertension can lead to persistent vascular injury and induce remodeling, namely stiffening and thickening in systemic arteries as an adaptation to elevated pressure (Humphrey, 2021; Zeng and Yang, 2024).

The vascular reactivity among Type 2 diabetic patients shows significant impairment as compared to healthy controls, as observed in several vascular response tests, including post-occlusive reactive hyperemia and endothelium-dependent and -independent vasodilation

responses (Caturano *et al.*, 2023). The impaired vascular reactivity has been closely associated with increased risks of target organ damage, generally considered the end-organ damage resulting from the long-term complications of hypertension, and, more importantly, both Type 2 diabetes and hypertension (Damanik and Yunir, 2021). The exposure to arterial hypertension results in a chronic, high mechanical stress environment for blood vessels, leading to vessel wall injury, thereby initiating structural changes in the arterial vessel (Mrugacz *et al.*, 2021). Perpetuating hypertension-induced vascular remodeling includes the deposition of structural proteins, thickening of the vascular wall, hypertrophy of smooth muscle cells, and reduction in the lumen area. As such, the normal vascular reactivity homeostasis is severely disrupted, which increases the prevalence of abnormal vascular responses related to vascular reactivity, including impaired vasodilation capacity and enhanced vasoconstriction at the early onset of Type 2 diabetes (Yousef *et al.*, 2023).

Vascular endothelial injury followed by vasodilation dysfunction at the reactivity level can have a profound impact downstream, disturbing the structural remodeling between heart and vessels, and ultimately leading to wide-ranged target organ damage in the retina, neurodystrophy, and kidney (Baaten *et al.*, 2023; Ray *et al.*, 2023). Moreover, oxidative stress and endothelial dysfunction are recognized as a common pathway affecting the vascular reactivity in the etiology of both diseases (Bhatti *et al.*, 2022). Therefore, preserving or restoring vascular health is of paramount importance in prevention and patient management in cases of Type 2 diabetes and hypertension (Barone *et al.*, 2021). Common therapeutic targets, such as cholesterol and antioxidants, are discussed as a potential avenue of future collaborations between different health professionals in hypertension and diabetes in order to promote vascular health (Lima *et al.*, 2022). Varied quantitative and qualitative interdisciplinary strategies for research to advance the understanding of vascular health among Type 2 diabetic patients and to evaluate its implication in disease prevention are outlined below to

illuminate the interconnectedness between metabolic disorders and a healthy vascular system (Kulkarni *et al.*, 2024; Pavlidou *et al.*, 2024).

Conclusion and Future Directions

The understanding of diabetes, hypertension, heart diseases, and the vascular system and their mutual interconnections has reached a significant point in recent years (Usman *et al.*, 2021). One methodical study explored and evaluated the complex relationship between diabetes and hypertension, diabetes and heart diseases, hypertension and heart diseases, and hypertension and the vascular system (Jyotsna *et al.*, 2023). Diabetes, hypertension, heart diseases, and the vascular system are very frequently interconnected (Zakir *et al.*, 2023). Some of the common risk factors for diabetes, hypertension, and heart diseases are increasing age, obesity, excessive alcohol consumption, and a high-fat diet, the last one of which causes high cholesterol (Jyotsna *et al.*, 2023).

The comprehensive literature review reviewed several articles on the relationships of diabetes, hypertension, heart diseases, and the vascular system (Wang *et al.*, 2021). The main need to appraise these relations is because on average there is a significant positive correlation (Tran *et al.*, 2021). On average, diabetes patients tend to get hypertension and heart diseases; drug-resistant high blood pressure is connected with heart failure; hypertension is likely to cause atherosclerosis (mainly due to reasons of vascular structures) (Studziński *et al.*, 2021). But in some special cases, the correlations may be negative (Nguyen *et al.*, 2021). There is only one gap; some articles on these connections come with relatively small sample sizes, which makes the results unreliable (Tsai *et al.*, 2021).

CONFLICT OF INTEREST

Authors hereby declare that they have no conflict of interest.

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