Review Article

Study of the Role of Oxidative Stress in Pathophysiology of Cardiovascular Diseases

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Abstract

Cardiovascular system is primarily considered as the human body's transport system. The cardiovascular system keeps life pumping through the body. Understanding the functions of the cardiovascular system, along with its various pathways of veins, arteries and capillaries, is essential in the provision of safe and effective care. Cardiovascular disease (CVD) remains to be the leading cause of premature deaths across the globe. Cardiovascular disease is an umbrella term for a number of linked pathologies. Cardiovascular diseases (CVD) are complex entities with heterogeneous pathophysiologic mechanisms and increased oxidative stress has been viewed as one of the potential common etiologies in various CVD. Oxidative stress in cardiovascular system may produce various cardiovascular diseases such as atherosclerosis, ischemic heart disease, and hypertension. In conclusion, oxidative stress is a condition that accompanies diseases of the cardiovascular system, and it may be responsible for the development of the disease or its complications, which must be taken into account in any treatment system.

Keywords: Cardiovascular system; Oxidative stress; Heart; Vessels; CVD

Introduction

Cardiovascular system is primarily considered as the human body's transport system. Oxygen, carbon dioxide, nutrients and other vital substances to the various tissues of human body are carried by the blood which circulates in a closed circulation [1]. The cardiovascular system has been comprised of a combination of several basic compartments, which are structurally connected to and functionally interact with each other [2]. The circulation of the heart and lungs (central circulation) and the rest of the body (peripheral circulation) form a single closed system with two components: an arterial system and a venous system. The arterial system carries blood from the heart and the venous system returns blood to the heart [3]. The cardiovascular system keeps life pumping through the body. Understanding the functions of the cardiovascular system, along with its various pathways of veins, arteries and capillaries, is essential in the provision of safe and effective care [4]. Cardiovascular disease remains to be the leading cause of premature deaths across the globe [5]. Heart illness (heart disease), peripheral artery disease, congenital and rheumatic heart diseases, cerebral vascular disease, and venous thromboembolism are all included under the term of CVD [6]. Although CVD may directly arise from different etiologies such as emboli in a patient with atrial fibrillation resulting in ischemic stroke, rheumatic fever causing valvular heart disease, among others, addressing risks factors associated to the development of atherosclerosis is most important because it is a common denominator in the pathophysiology of CVD [7]. Oxidative stress is defined as an imbalance in the balance between antioxidants and pro-oxidants in favor of antioxidants [8]. Antioxidants play a major role in protecting against molecular oxidative

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damage [9]. Indeed cardiovascular system exposes too many complications that can be related to an oxidative stress that is also associated with the appearance of several pathologies [10]. In the current review study, the aim was to evaluate the role of oxidative stress in cardiovascular system disorders.

Heart

The heart is a muscular organ about the size of a fist. With every heartbeat, the heart pumps blood that carries oxygen and nutrients to all parts of the body [11]. The atria are upper receiving chambers for returning venous blood. The ventricles comprise most of the heart's volume, lie below the atria, and pump blood from the heart into the lungs and arteries [12]. The heart is a hollow located in the chest between the lungs behind the sternum and above the diaphragm. It is surrounded by the pericardium [13]. The heart is usually positioned within the mediastinum with one-third of its mass to the right of the midline, and with its own long axis directed from the right shoulder towards the left hypochondrium [14] (Figure 1).

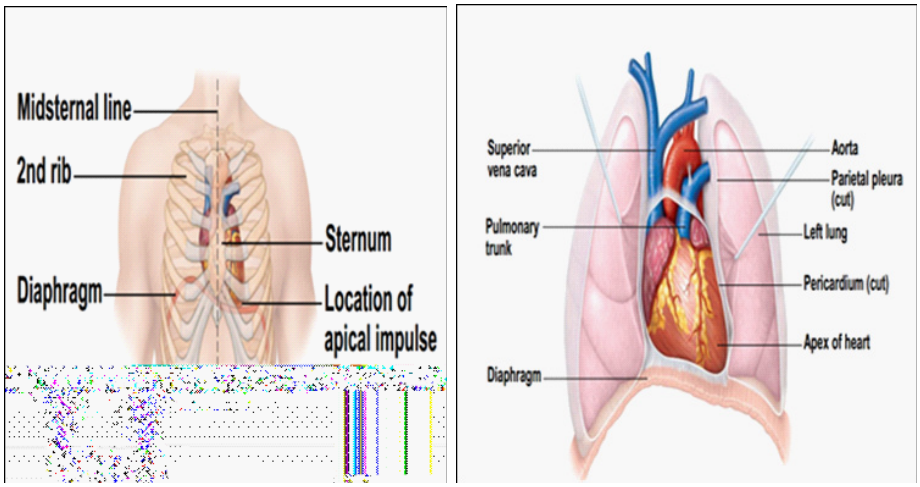

Figure 1: Situation of the Heart [15]

Anatomical description

The heart is primarily a muscular pump and possesses many muscle fibres. Atria and ventricles have a different microstructural organization; also, heart valves and ventricle walls possess a different microstructure [16]. Heart is a fibroserous sac comprising three concentric layers [17] with diverse structure and function (Figure 2). The inner layer endocardium and the outer layer epicardium are both very thin, each being about 100 µm thick; the middle layer, called myocardium, constitutes the bulk of the cardiac tissue and endows it with the ability to pump blood [16].

Blood vessels

There are three types of blood vessels: arteries, capillaries and veins. These are the pipes which distribute the blood throughout the body. The lumen is the channel within blood vessels which allows blood to flows [19].

Arteries are the big, thick-walled vessels that transport blood away from the heart. A thick layer of smooth muscle lines the inside of arteries, and this muscle can contract or relax, contributed to change the size of the arterial lumen. There are three subtype the largest artery is the aorta then the coronary arteries and the smallest one is the arterioles [20, 21].

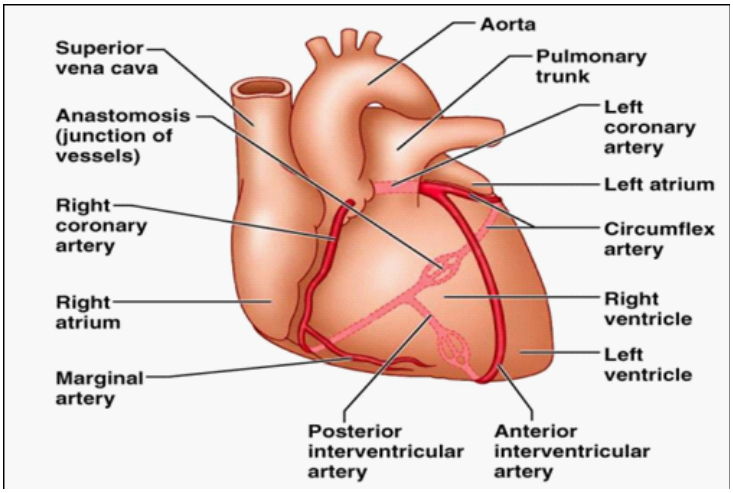

Figure 2: Anatomy of the Heart [18]

Cardiovascular disease

Globally, cardiovascular disease continues to be the primary cause of early mortality [24]. Cardiovascular disease is a term for a number of linked pathologies, commonly defined as coronary heart disease (CHD), cerebrovascular disease, and congenital heart diseases; venous thromboembolism [25]; Heart failure (HF); Hypertension (HTN); Cerebral vascular accident (CVA) which is stroke: hemorrhagic, ischemic or transit ischemic attack; Rheumatic heart disease; Peripheral vascular accident (PAD) which is lower extremity artery disease (LEAD), aortic aneurysm and Interventricular communication. As a harrowing statistic, every 39 seconds someone dies due to cardiovascular disease, claiming more lives than cancer in the United States [26].

Cardiovascular disease and oxidative stress

There are several potential sources of ROS in the heart, including mitochondria, nitric oxide synthases (NOSs), NADPH oxidase, and monoamine oxidases (Table 1).

Table 1: Potential sources of ROS in the heart [27-30].

Mitochondrial ROS	(i) Complexes I and III are the best characterized enzyme complexes mediating ROS generation in the mitochondria and are responsible for the majority of mitochondrial ROS in cardiovascular physiology anddisease. (ii) Mitochondrial oxidant modifications attenuate cardiac aging, protect from cardiac disease, and prevent left ventricular remodeling and failure in animal models. (iii) The increased mitochondrial calpain-1 is associated with mitochondrial ROS generation in diabetic cardiomyopathy (iv) Mitochondrial ROS affect a broad range of cellular functions in the context of heart failure.
NADPH oxidases (Nox)	(i) Nox activity increases in the failing heart and in angiotensin-II-induced cardiac hypertrophy. (ii) Suppression of Nox2 and Nox4 below physiological levels is able to exacerbate myocardial I/R injury, whereas a minimum level of ROS production by either Nox2 or Nox4 is essential for the activation of hypoxia-inducible factor-1α (HIF-1α) and inhibition of PPARα during I/R. (iii) ROS generated by the Nox family of NADPH oxidases may act as second messengers regulating cell growth and differentiation. (iv) ROS specifically derived from the Nox2 NADPH oxidase give a relevant contribution to the development of cardiac remodeling associated with chemotherapy-induced cardiotoxicity

NOSs	(i) nNOS-derived NO may inhibit XOR activity, limiting myocardial oxidative stress and increasing NO availability within the myocardium. (ii) O 2- from Nox may activate XOR and degrade BH 4 leading to NOS uncoupling, as observed in diabetes and hypertension (iii) Pressure overload triggers eNOS uncoupling, which in turn contributes to dilatory remodeling and cardiac dysfunction. (iv) iNOS up-regulation and overexpression induce cardiac apoptosis, fibrosis, hypertrophy, and dilatation inanimal models.
Monoamineoxidases (MAO)	(i) MAO-dependent oxidative stress also contributes to mast cell degranulation and cardiac fibrosis, ultimatelyresulting in diastolic dysfunction in type 1 diabetes. (ii) MAO activity is associated with an increased risk for POAF. (iii) Genetic deletion of MAO-B protects against oxidative stress, apoptosis, and ventricular dysfunction. (iv) Genetic deletion of MAO-A is protective in I/R injury, pressure overload, and heart failure.

Cardiovascular diseases (CVD) are complex entities with heterogenous pathophysiologic mechanisms and increased oxidative stress has been viewed as one of the potential common etiologies. Increased oxidative stress has been viewed as one of the potential common etiologies in various CVD [31]. Oxidative stress in cardiovascular system may produce various cardiovascular diseases such as atherosclerosis, ischemic heart disease, hypertension, congestive heart failure, cardiac hypertrophy and cardiomyopathies by producing cell injury to cardiovascular tissue [32].

In pathological situations, ROS are able to cause oxidative modification of major cellular macromolecules (such as lipids, proteins, or DNA). This oxidation induces modifications in subcellular organelles such as sarcolemma, mitochondria, sarcoplasmic reticulum, and nucleus. As an example, ROS could modulate contractility by oxidation of sarco/endoplasmic reticulum Ca2+-ATPase (SERCA 2A) and contractile proteins such as tropomyosin and actin, leading to contractile dysfunction [33] (Figure 3).

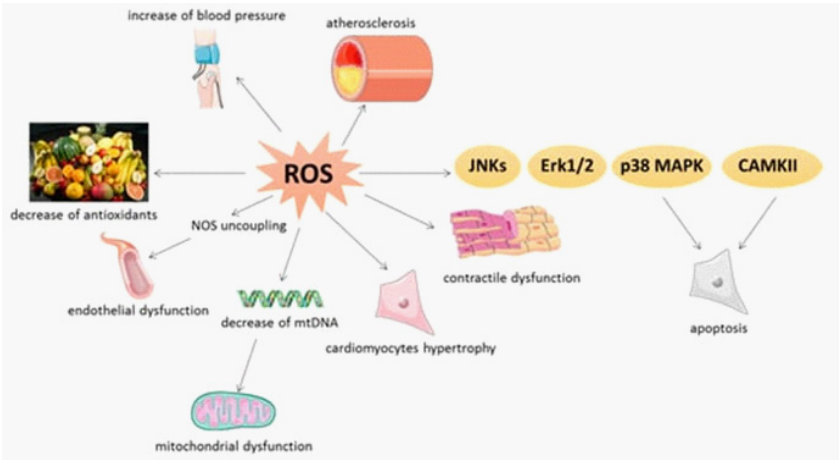

Figure 3: Pathological roles of oxidative stress and ROS in cardiovascular tissues [33]

In animal models, oxidative stress plays a crucial role in hypertension. Statin treatment of spontaneously hypertensive rats resulted in a decrease in O2 generation and AT1-receptor activation as well as a corresponding drop in blood pressure. [34]. In mice, the chimeric gp91ds-Tat peptide that prevents NAD(P)H oxidase activation also reduced the generation of ROS and elevated blood pressure caused by Ang II. In rat models, hypertension has also been linked to oxidative stress brought on by increased 12-LO. This implies that hypertension is caused by a variety of oxidative processes [35]. In the other hand,

TNF-α and Ang II caused hypertrophy in rat heart myocytes in a ROS-dependent way; antioxidant usage, such as catalase, vitamin E, and butylated hydroxyanisole, avoided this.74 Catalase overexpression greatly suppressed Ang II-induced hypertrophy, and antisense p22phox transfection prevented Ang II-induced H2O2 production [36]. This indicates that the hypertrophy was caused by oxidative stress mediated by NAD(P)H oxidase.75 NAD(P)H oxidase-dependent ROS generation markedly and gradually increased during compensated hypertrophy in a guinea pig model, peaking at the level of decompensated heart [37]

Conclusion

Cardiovascular diseases are multifaceted conditions with diverse etiologies. Cardiovascular illnesses are frequently accompanied by oxidative stress, which should be considered in any treatment plan since it may contribute to the onset of the disease or its complications. A deeper comprehension of ROS-dependent signal transduction events, their locations, and the integration of ROS-dependent transcriptional and signaling pathways in vascular pathophysiology are necessary for the development of effective pharmaceutical therapeutics for CVD.

References

1. Chetehouna S, Atoussi O, Boulaares, Guemari I Y, Derouiche S. The effect of Chronic Tobacco smoking on Atherogenic index and Cardiovascular diseases risk in El-Oued (Algeria) men. Asian J. Research Chem. 2020; 13(6): 1-6.
2. Atoussi O, Chetehouna S, Boulaares I, Guemari I Y, Derouiche S. Analysis of Blood Pressure, Lipid Profile and Hematological Biomarkers in men Addicted to Tobacco Chewing. Research Journal of Pharmacology and Pharmacodynamics. 2021; 13(1): 1-6.
3. Jain V, Bordes SJ, Bhardwaj A. Physiology, Pulmonary Circulatory System. 2023. Treasure Island Available from: https://www.ncbi.nlm.nih.gov/books/NBK525948/
4. Syed F, Khan S, Toma M. Modeling Dynamics of the Cardiovascular System Using Fluid-Structure Interaction Methods. Biology. 2023; 12(7):1026. https://doi.org/10.3390/biology12071026
5. Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study [published correction appears in J Am Coll Cardiol. 2021 Apr 20;77(15):1958-1959. doi: 10.1016/j.jacc.2021.02.039]. J Am Coll Cardiol. 2020; 76(25):2982-3021. doi:10.1016/j.jacc.2020.11.010
6. Stewart J, Manmathan G, Wilkinson P. Primary prevention of cardiovascular disease: A review of contemporary guidance and literature. JRSM Cardiovasc Dis. 2017;6:2048004016687211. Published 2017 Jan 1. doi:10.1177/2048004016687211
7. Fox CS, Coady S, Sorlie PD, Levy D, Meigs JB, D'Agostino RB, Wilson PW, Savage PJ. Trends in cardiovascular complications of diabetes. JAMA. 2004 Nov 24; 292(20):2495-9.
8. Derouiche S, Chetehouna S, Atoussi W. "The Effects of aqueous leaf extract of Portulaca oleracea on haemato-biochemical and histopathological changes induced by Sub-chronic Aluminium toxicity in male wistar rats." Pharmacological Research-Modern Chinese Medicine (2022): 100101.
9. Boulaares I, Derouiche S, Niemann J. Ocimum basilicum L.: A Systematic Review on Pharmacological Actions and Molecular Docking Studies for Anticancer Properties. J Biochem Technol (2024) 15(1): 12-18
10. Steven S, Frenis K, Oelze M. Vascular Inflammation and Oxidative Stress: Major Triggers for Cardiovascular Disease. Oxid Med Cell Longev. 2019;2019:7092151. Published 2019 Jun 23. doi:10.1155/2019/7092151
11. Yousef M, Sulieman A, Edward C, Ahmed B. A Review on Diagnostic Procedures for the

Cardiovascular System. International Journal of Science and Research (IJSR), 2013; 2(2): 535-542.

12. Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. Frontiers in Psychology, 2014; 5: 1-19. DOI: 10.3389/fpsyg.2014.01040.
13. Hussein MU. Chapter1: Medical Physics. Physics and The Cardiovascular System. 2017
14. Anderson RH, Razavi R, Taylor A M. Cardiac anatomy revisited. J. Anat. 2004; 205: 159–177.
15. Heard B. Atlantic Cape Community College. 2013
16. Tringelova M, Nardinocchi P, Teresi L, Di-Carlo A. The cardiovascular system as a smart system. 2007; 10: 12-19. DOI:10.1142/9789812706874_0018
17. Mahadevan V. Anatomy of the heart. Surgery. 2018; 36(2), 43-47. doi:10.1016/j.mpsur.2017.11.010.
18. Ebneshahidi A. THE HEART, Pearson Education: Inc., publishing as Benjamin Cummings. 2006
19. Hammadi M, Derouiche S. A study on the prevalence and risk factors of coronary artery disease in patients with metabolic syndrome infected and not infected with COVID 19 from El-Oued (Algeria) region Biomedicine: 2024; 44(1): 89-95. DOI: https://doi.org/10.51248/.v44i1.4123
20. Brozovich FV, Nicholson CJ, Degen CV, Gao YZ, Aggarwal M, Morgan KG. Mechanisms of Vascular Smooth Muscle Contraction and the Basis for Pharmacologic Treatment of Smooth Muscle Disorders. Pharmacol Rev. 2016;68(2):476-532. doi:10.1124/pr.115.010652
21. Villa AD, Sammut E, Nair A, Rajani R, Bonamini R, Chiribiri A. Coronary artery anomalies overview: The normal and the abnormal. World J Radiol 2016; 8(6): 537-555. DOI: 10.4329/wjr.v8.i6.537
22. Satish M, Tadi P. Physiology, Vascular. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542252/
23. Miller LM, Gal A. Cardiovascular System and Lymphatic Vessels. Pathologic Basis of Veterinary Disease. 2017;561-616.e1. doi:10.1016/B978-0-323-35775-3.00010-2
24. Hasani WSR, Muhamad NA, Hanis TM, et al. The global estimate of premature cardiovascular mortality: a systematic review and meta-analysis of age-standardized mortality rate. BMC Public Health. 2023;23(1):1561. doi:10.1186/s12889-023-16466-1.
25. Stewart J, Manmathan G, Wilkinson P. Primary prevention of cardiovascular disease: A review of contemporary guidance and literature. JRSM Cardiovasc Dis. 2017;6:2048004016687211. doi:10.1177/2048004016687211.
26. Yuyun MF, Sliwa K, Kengne AP, Mocumbi AO, Bukhman G. Cardiovascular Diseases in Sub-Saharan Africa Compared to High-Income Countries: An Epidemiological Perspective. Glob Heart. 2020;15(1):15. doi:10.5334/gh.403
27. D'Oria R, Schipani R, Leonardini A, Natalicchio A, Perrini S, Cignarelli A, Laviola L, Giorgino F. The Role of Oxidative Stress in Cardiac Disease: From Physiological Response to Injury Factor. 2020; ID 5732956: 29 pages https://doi.org/10.1155/2020/5732956.
28. Boulaares I, Derouiche S, Guemari IY. Protective effect of ObE against Doxorubicin-Induced immunosuppression and Cardiotoxicity in Rats. Research J. Pharm. and Tech. 2024; 17(4):1839-1843.
29. Boulaares I, Derouiche S, Guemari IY, Impact of Doxorubicin Chemotherapy on Oxidative Stress Status in Heart and Liver: An experimental Study on Rats. Pharma Sci Analytical Res J 2024; 6(3):

180067.

30. Chetehouna S, Boulaares I, Atoussi O, Guemari IY, Derouiche S. Green Nanoparticles as a Novel Application of Nanotechnology in Medicine: Study of zinc, Copper and Magnesium Nanoparticles. Rec. Pharm. Biomed. Sci. 2024; 8 (3), 109-120.
31. Senoner T, Dichtl W. Oxidative Stress in Cardiovascular Diseases: Still a Therapeutic Target?. Nutrients. 2019; 11(9):2090. doi:10.3390/nu11092090.
32. Panda P, Verma HK, Lakkakula S, et al. Biomarkers of Oxidative Stress Tethered to Cardiovascular Diseases. Oxid Med Cell Longev. 2022;2022:9154295. doi:10.1155/2022/9154295.
33. Dubois-Deruy E, Peugnet V, Turkieh A, Pinet F. Oxidative Stress in Cardiovascular Diseases. Antioxidants. 2020; 9(9):864. https://doi.org/10.3390/antiox9090864
34. Amponsah-Offeh M, Diaba-Nuhoho P, Speier S, Morawietz H. Oxidative Stress, Antioxidants and Hypertension. Antioxidants (Basel). 2023;12(2):281. doi:10.3390/antiox12020281
35. Zhang Y, Murugesan P, Huang K, Cai H. NADPH oxidases and oxidase crosstalk in cardiovascular diseases: novel therapeutic targets. Nat Rev Cardiol. 2020;17(3):170-194. doi:10.1038/s41569-019-0260-8
36. Sriramula S, Francis J. Tumor Necrosis Factor - Alpha Is Essential for Angiotensin II-Induced Ventricular Remodeling: Role for Oxidative Stress. PLoS One. 2015;10(9):e0138372. doi:10.1371/journal.pone.0138372
37. Boulaares I, Derouiche S, Niemann J. HPLC-Q-TOF-MS analysis of phenolic compounds, in vitro biological activities and in vivo acute toxicity evaluation of Ocimum Basilicum L. Fresenius Environmental Bulletin. 2024; 33(2): 73-82.