|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author/****Year** | **Country** | **Title** | **Type of Study** | **Objectives** | **Methods** | **Main findings** |
|  Emelyanova, L.; 2016[15] | USA | Selective downregulation of mitochondrial electron transport chain activity and increased oxidative stress in human atrial fibrillation | Case-control | The study compared mitochondrial oxidative phosphorylation (OXPHOS) complexes and oxidative stress in right atrial tissue between non-AF and AF patients undergoing open-heart surgery. | Between 2012 and 2016, elective open-heart surgery patients were examined for atrial appendage tissues, examining factors like O2 oxidoreductase activity, mitochondrial OXPHOS complexes, citrate synthase activity, and protein expression. | AF is linked to decreased ETC activity and increased oxidative stress, which can contribute to the progression of the substrate for AF. |
| Muszyński, P.; 2021[28] | Switzerland | Mitochondrial dysfunction in atrial fibrillation— mechanisms and pharmacological interventions | Review | This review examines mitochondrial dysfunction linked to atrial fibrillation and discusses pharmacological treatments targeting mitochondria to prevent or enhance atrial fibrillation outcomes. | This text aims to comprehend the pathophysiological mechanism of arrhythmia, its prevention methods, and the role of mitochondrial dysfunction in the onset of arrhythmia. | Mitochondrial dysfunction, a key factor in cardiomyocyte integrity and cardiac performance, can be addressed through medications that target energetic imbalance, metabolic disturbance, and oxidative stress. |
| Ren, X.; 2018[29] | China | Mechanisms and treatments of oxidative stress in atrial fibrillation | Review | This review examines mitochondrial dysfunction linked to atrial fibrillation and discusses pharmacological treatments targeting mitochondria to prevent or enhance atrial fibrillation outcomes. | The research uses atrial electrical and structural remodeling data to explore various reactive oxygen species pathways that can induce atrial fibrillation (AF). | AF-related oxidative stress, triggered by factors like NADPH oxidase activation, calcium overload, and cardiovascular conditions, maybe a therapeutic target for AF. |
| Korantzopoulos, P. 2007[30] | Greece | The role of oxidative stress in the pathogenesis and perpetuation of atrial fibrillation | Review Article | This summary critically analyzes the current literature on AF and oxidative stress, highlighting the scientific background of antioxidant therapeutic interventions. | The authors conducted a comprehensive search using the MEDLINE database, reference lists, and significant cardiovascular journal supplements to identify studies published up to December 2005. | Oxidative stress is linked to AF pathophysiology, contributing to arrhythmia perpetuation. Modulating oxidative stress can benefit AF's development of inflammatory and electrophysiological changes. |
| Schillinger, K. J.; 2012[31] | USA | Atrial fibrillation in the elderly: The potential contribution of reactive oxygen species | Review | The study explores the link between aging and Alzheimer's disease (AF) through reactive oxygen species (ROS) oxidative damage, which induces intracellular and extracellular changes. | Overview of AF pathophysiology and introduces the critical structures that predispose an otherwise healthy atrium to AF when damaged. The available evidence that ROS can lead to damage to these vital structures is then reviewed. Finally, the evidence linking the aging process to the pathogenesis of AF is discussed. | To be certain, through serving as agents of oxidative cellular damage, ROS is likely to be a major causative factor in the development of AF. The cellular changes brought about by ROS-mediated damage are sufficient to promote tissue changes consistent with AF triggers and atrial electrical and structural remodeling. |
| Mason, F. E.; 2020[32] | Germany | Cellular and mitochondrial mechanisms of atrial fibrillation | Review | This review discusses the importance of mitochondrial Ca2+ handling in regulating ATP production and mitochondrial ROS emission and how alterations may play a role in AF, particularly in these aspects of mitochondrial activity. | It is understanding the molecular mechanisms underlying AF and specific treatment options. | In the current review, we discussed a hypothesis that remodeling and increased energy demand during AF lead to oxidative stress, shifting the redox environment to a state of energy deficit and compromised ROS scavenging capacity. |
| Mascolo, A.; 2020 (34) | Italy | Angiotensin II and angiotensin 1–7: which is their role in atrial fibrillation? | Review | This review aims to provide an overview of the evidence for the possible role of the two RAS pathways (classic and non-classic) in the pathophysiology of AF, the proposed cellular and molecular mechanisms, and the results of clinical studies with classic RAS antagonists. | Understand the role of the RAS in the induction of AF, influenced by inflammatory and cardiac processes, electrical remodeling, and epicardial fat accumulation. | In this review, we summarized the evidence showing that both RAS pathways can balance the onset of AF through different biological mechanisms involving inflammation, epicardial adipose tissue (EAT) accumulation, and cardiac remodeling. |
| Tribulova, N.; 2015(36) | Slovak Republic | New aspects of the pathogenesis of atrial fibrillation: Remodeling of intercalated discs | Review | Understanding of the role of key factors of aging, oxidative stress, and inflammation in the development of age-related cardiovascular disease and FA. | Review of reactive oxygen species, their production, and relationship with systemic inflammation. Approach to studies that consider cardiac structural and electrophysiological remodeling as crucial for developing and maintaining atrial fibrillation. | Data suggest that alterations in atrial connexin-43 and/or connexin-40 expression, phosphorylation, and distribution affect cell-to-cell electrical coupling and molecular signaling that is proarrhythmogenic. Gap junctional connexin channels are considered targets for arrhythmia prevention, and therapeutic interventions for mitochondria-related reactive oxygen species appear. In addition, aging is accompanied by abnormalities in adhesive junctions that most likely promote asynchronous contraction and arrhythmias. |
| Pool, L.; 2021[37] | Switzerland | The role of mitochondrial dysfunction in atrial fibrillation: Translation to druggable target and biomarker discovery | Review | To dissect molecular mechanisms that drive AF. To investigate the role of mitochondrial impairment in AF may guide the path towards new therapeutic and diagnostic targets. | Review of the molecular mechanisms that drive AF and the genesis of this clinical situation | Novel findings show a key role for mitochondrial dysfunction in the onset and progression of AF. Current therapeutic strategies for AF are aimed directly at the suppression of AF symptoms but are not effective in terms of preventing AF progression. Furthermore, no AF-specific biomarkers are available. So far, several mitochondrial biomarkers have been tested in clinical AF. Recent findings indicate the potential diagnostic value of blood-based 8-OHdG and cfc-mtDNA in staging AF. |
| Kim, Y. H., 2003[38] | Korea | Gene expression profiling of oxidative stress on atrial fibrillation in humans | Case-control | The study aims to examine the gene transcriptional profiles in human myocardial tissues under AF and oxidative stress conditions. | Researchers studied the effects of oxidative stress on atrial fibrillation (AF) using radioactive DNA microarrays to evaluate changes in gene expression in 26 AF patients undergoing the Maze procedure. | Gene expression profiles reveal 30 upregulated and 25 downregulated genes in AF patients, with five ROS-related genes increasing by over 2.0 and two antioxidant genes decreasing. |
| Van Wagoner, D. R, 2008[39] | USA | Oxidative stress and inflammation in atrial fibrillation: Role in pathogenesis and potential as a therapeutic target | Review | The study explores the potential of therapeutic intervention in manipulating oxidative and inflammatory pathways. | This review examines the various treatments for AF utilizing ion channel blockade and the fundamental mechanisms that underlie AF. | AF is a multifactorial arrhythmia characterized by rapid atrial contractile activity degradation, blood stasis, thrombus formation, and increased electrical instability due to aging and other risk factors. |
| Liu2015[40] | China | Serum levels of nicotinamide adenine dinucleotide phosphate oxidase 4 are associated with non-valvular atrial fibrillation. | Clinical study | The present study aimed to investigate the potential association between serum levels of NOX4 and inflammatory biomarkers and AF. | The study involved 180 consecutive AF patients admitted to Tianjin Medical University's Department of Cardiology between 2012 and 2013, with a final population of 108 successive AF patients. | The study indicates a correlation between elevated NOX4 levels and AF, indicating a potential role of NOX4 in the pathophysiology of human AF. |
| Cangemi, 2009[41] | Italy | Different behavior of NOX2 activation in patients with paroxysmal/persistent or permanent atrial fibrillation | Case-control | To define the role of NOX2 and isoprostanes, a marker of oxidative stress, in the different settings of AF. | A study involving 174 patients with atherosclerosis (AF) and 90 controls was conducted, measuring urinary isoprostanes and serum levels of soluble NOX2-derived peptides. | Patients with paroxysmal/persistent AF had higher urinary isoprostanes and sNOX2-dp concentrations than permanent AF and controls, with baseline values independently associated with AF type. |
| David Bode2021[42] | Germany | Implications of SGLT Inhibition on Redox Signalling in Atrial Fibrillation | Review | The study evaluates the implications of SGLT inhibition on redox signaling in AF. | This study involved a review of clinical data and trials, exploring the association between diabetes, AF, and the use of SGLTi. | The study findings indicate that SGLTi has potential benefits in reducing AF burden. |
| Ryo Nishinarita, 2021[43] | Japan | Canagliflozin Suppresses Atrial Remodeling in a Canine Atrial Fibrillation Model | Experimental study | The study explored the potential benefits of Canagliflozin (CAN) and other SGLT2 inhibitors in preventing atrial fibrillation (AF) and inhibiting atrial remodeling promotion. | The study involved 12 beagle dogs, 10 undergoing rapid atrial pacing, and compared their performance over three weeks, analyzing parameters and histological findings. | CAN treatment reduces atrial-effective refractory period, conduction velocity, and atrial artery disease (AF) incidence, mitigating interstitial fibrosis and oxidative stress in atrial tissues. |
| Takuya Koizumi; 2023[44] | Japan | Empagliflozin suppresses mitochondrial reactive oxygen species generation and mitigates the inducibility of atrial fibrillation in diabetic rats. | Experimental study | The study investigated the potential of empagliflozin to reduce mitochondrial reactive oxygen species (ROS) generation and reduce fibrosis in diabetic patients, considering the correlation between oxidative stress and AF pathogenesis. | The study examined the effects of empagliflozin on atrial mitochondrial respiratory capacity, reactive oxygen species generation, oxidative stress markers, protein expression, atrial tachyarrhythmia inducibility, and fibrosis in a type-2 diabetes model. | The study suggests empagliflozin may have cardioprotective effects by reducing mitochondrial ROS generation in diabetic rats' atrium, potentially suppressing the development of atrial fibrillation (AF) in type-2 diabetes. |
| Alana Aragón-Herrera, 2022[46] | Spain | Relaxin-2 plasma levels in atrial fibrillation are linked to inflammation and oxidative stress markers. | Case-control | The study investigates the correlation between relaxin-2 plasma levels in the left atrium and peripheral vein with fibrosis, inflammation, and oxidative stress in AF patients and its anti-fibrotic properties. | The study involved 68 Caucasian patients with persistent AF who underwent pulmonary vein radiofrequency catheter ablation at the University Clinical Hospital of Santiago de Compostela. | Patients with higher relaxin-2 concentrations in peripheral veins had higher Gal-3 levels in plasma, and RLX2 treatment reduced mRNA expression levels in NHCF-A cells. |
| Yushu Liu; 2023[47] | China | Costunolide ameliorates angiotensin II-induced atrial inflammation and fibrosis by regulating mitochondrial function and oxidative stress in mice: A possible therapeutic approach for atrial fibrillation. | Experimental study  | The study examines the positive impact of costunolide on angiotensin 2-induced atrial fibrillation. | Male C57BL/6 mice induced with AF using Ang II were administered varying doses of Costunolide (COS) for three weeks. | Costunolide has shown potential therapeutic benefits in treating Angiotensin II-induced atrial fibrillation by reducing inflammation, fibrosis, and mitochondrial dysfunction. |
| DongZhu Xu; 2021[48] | Japan | Xanthine oxidase inhibitor febuxostat reduces atrial fibrillation susceptibility by inhibition of oxidized CaMKII in Dahl salt-sensitive rats | Experimental study | The study evaluated the impact of febuxostat, an XO inhibitor, on salt-induced hypertension in a rat model compared to allopurinol.  | Researchers studied Dahl salt-sensitive rats on high-salt diets, dividing them into three groups and administering treatments orally. They measured blood pressure, atrial fibrillation, and protein expression. | Febuxostat and allopurinol significantly reduced hypertension-related atrial fibrillation in rats, improving calcium handling. XO inhibitors reduced Ca2+ handling protein expression and partially restored connexin 40 expressions. |
| Yong-Yan Fan; 2019[49] | China | Effects of febuxostat on atrial remodeling in a rabbit model of atrial fibrillation induced by rapid atrial pacing  | Experimental study | The study evaluated the impact of febuxostat on atrial remodeling in a rabbit model of atrial fibrillation (AF) induced by rapid atrial pacing and explored its mechanisms. | Rabbits were divided into four groups, each with different RAP levels. Effects of febuxostat on atrial remodeling, inflammation, oxidative stress markers, and left atrium signaling pathways were examined. | Rapid atrial pacing in rabbits leads to atrial enlargement, dysfunction, and fibrillation, while Febuxostat treatment suppresses these changes by inhibiting atrial electrical and structural remodeling. |
| Mengqi Gong;2020[50] | China | Wenxin Keli Regulates Mitochondrial Oxidative Stress andHomeostasis and Improves Atrial Remodeling in Diabetic Rats | Experimental study | This study evaluated the hypothesis that WXKL can improve atrial remodeling in diabetic rats, restoring mitochondrial function. | Primary cultures of atrial fibroblasts isolated from neonatal Sprague-Dawley (SD) rats were used. Male SD rats were divided into control, DM (diabetes mellitus), and DM + WXKL (WXKL treatment) groups. Diabetes induction was performed by injection of STZ, followed by treatment with WXKL.  | WXKL prevents oxidative stress and improves mitochondrial function. In diabetic rats treated with WXKL, several parameters were improved, including atrial fibrosis, reduced atrial diameter, increased atrial conduction velocity, and reduced induction of atrial fibrillation. |
| Pengcheng YU; 2023[51] | China | Andrographolide protects against atrial fibrillation by alleviating oxidative stress injury and promoting impaired mitochondrial bioenergetics. | Experimental study | This study aimed to explore the mechanisms of action of andrographolide to AF. | The study investigated Andr's role in atrial fibrillation (AF) by pre-treating HL-1 cells and rabbits with Andr before RES and atrial pacing using RNA sequencing. | Andrographolide effectively mitigates rapid atrial pacing, causing changes in electrophysiology, inflammation, oxidative damage, and apoptosis, potentially through a therapeutic mechanism involving the Keap1-Nrf2 complex. |
| Alicja Bukowska, 2007[54] | Germany | Mitochondrial dysfunction and redox signaling in atrial tachyarrhythmia | Case-control | The study investigates the impact of AF on mitochondrial dysfunction and oxidative stress-activated signal transduction by analyzing NF-kB, LOX-1, ICAM-1, and HO-1. | Ex vivo atrial tissue from patients with and without atrial fibrillation was studied for mitochondrial structure and respiration, while NF-kB target gene expression was measured using various methods. | Oxidative stress, mitochondrial structure, and respiration were observed in human atrial tissue slices, with NF-jB accumulation and elevated ICAM-1 expression. A blockade with verapamil prevented these changes. |
| Hadi, H. A.; 2010[55] | United Arab Emirates | Inflammatory cytokines and atrial fibrillation: current and prospective views | Post-hoc comparison of data collected in a prospective randomized investigation | To present an overview of the evidence linking inflammatory cytokines to AF. | The authors analyzed articles published until December 2009 on Medline, Pubmed, Scopus, and EBSCOhost® using indexing terms for inflammation, cytokines, AF, and atrial arrhythmias. | Inflammatory cytokines and markers like IL-6 and CRP are linked to atrial fibrillation (AF), potentially indicating inflammation and predicting thromboembolic events in AF patients. |
| Zhiqiang Zhao; 2020[56] | China | Attenuation of atrial remodeling by aliskiren via affecting oxidative stress, inflammation and PI3K/Akt signaling pathway | Experimental study | The study investigates the cardioprotective effect of aliskiren (ALS) and its potential molecular mechanisms in atrial remodeling, focusing specifically on atrial fibrillation (AF). | The study involved acute and chronic experiments on dogs subjected to rapid atrial pacing, assessing parameters like effective refractory periods, AF inducibility, and average duration. | Aliskiren has shown cardioprotective effects by reducing electrophysiological alterations, oxidative stress, inflammation, and atrial remodeling, possibly through regulating the PI3K/Akt signaling pathway. |
| Xiaofei Xue; 2020 (60) | China | Exogenous hydrogen sulfide reduces atrial remodeling and atrial fibrillation induced by diabetes mellitus via activation of the PI3K/Akt/eNOS pathway. | Experimental study | This study aimed to explore the impact of hydrogen sulfide on diabetes mellitus-induced atrial fibrillation and its underlying mechanism.  | The study involved Sprague-Dawley rats in four groups: control, DM, H2S, and DM+H2S, analyzing atrial fibrillation, fibrosis, protein expression, cell viability, and cardiac fibroblast migration. | H2S may reduce atrial fibrosis and DM-induced AF by activating the PI3K/Akt/eNOS pathway. |
| Li, J.; 2010(62) | EUA | Role of inflammation and oxidative stress in atrial fibrillation | Case-control | The study aims to understand the role of inflammation and oxidative stress in developing AF. | A study compared 305 AF patients with and without AF, assessing serum inflammatory markers and oxidative stress and comparing them to control patients. | IL-6, IL-8, IL-10, TNF-α, MCP1, VEGF, and NTpBNP concentrations were linked to AF, with graded increases in TNF-α and NTpBNP among paroxysmal, persistent, and permanent AF subgroups. |
| Katarina Andelova; 2022(63) | Slovakia | Mechanisms Underlying Antiarrhythmic Properties of Cardioprotective Agents Impacting Inflammation and Oxidative Stress | Review  | The study aimed to examine the antiarrhythmic efficacy and molecular mechanisms of current clinically used pharmaceuticals in the context of AF. | The study examines the biomolecular mechanisms of FA and the therapeutic efficacy of Sodium-Glucose Cotransporter-2 Inhibitors, Statins, and Omega-3 fatty acids in preventing oxidative and inflammatory stress. | The approach suggests that reducing oxidative and inflammatory stress can eliminate pro-arrhythmic factors and arrhythmia substrates, making it a potent tool for reducing cardiac arrhythmia burden. |
| Han, W.; 2008(64) | China | Nitric oxide overproduction derived from inducible nitric oxide synthase increases cardiomyocyte apoptosis in human atrial fibrillation. | Case-control | The study aims to investigate the potential role of iNOS in atrial remodeling in AF. | The study investigated patients with permanent AF and sinus rhythm after mitral valve replacement surgery, using Western blotting, immunohistochemical staining, and NOX Detection Kit to measure cardiac function. | NOS expression in the right atrium was upregulated, while eNOS did not. Inflammation and oxidative damage in the right atrium of AF patients were associated with increased iNOS/eNOS expression. |
| Bukowska, A.; 2010(65) | Germany | Atrial expression of endothelial nitric oxide synthase in patients with and without atrial fibrillation | Case-control | The study aims to assess the endocardial expression of eNOS in atrial tissue samples from patients with and without atrial fibrillation (AF). | Tissue microarrays were used to analyze atrial tissue from 234 patients, examining differences in atrial eNOS expression, with immunohistological results confirmed by Western blotting in selected patients. | eNOS expression is influenced by factors like diabetes mellitus and coronary artery disease, with women with AF having the lowest levels. |
| Neuman, R. B.; 2007(66) | USA | Oxidative stress markers are associated with persistent atrial fibrillation. | Cross-sectional study | To compare serum markers of oxidation and associated inflammation in individuals with or without AF. | A cross-sectional study compared serum markers of oxidative stress and inflammation in 40 males with or without AF, matched by age, sex, diabetes, and smoking status. | Oxidative stress, not inflammatory markers, is statistically associated with AF, suggesting that oxidative stress markers may be predictive in AF management. |
| Pinho-Gomes, A. C.; 2014(67) | United Kingdom | Targeting inflammation and oxidative stress in atrial fibrillation: Role of 3-hydroxy-3-methylglutaryl-coenzyme a reductase inhibition with statins | Review | Using statins to decrease inflammation by restoring the myocardial nitroso-redox balance. | This review explores articles discussing potential statin-related therapies and their potential to reduce inflammation. | Statins show the highest anti-arrhythmic benefits in preventing postoperative AF but limited benefits in primary AF prevention, making them unsuitable for preventing incident AF or recurrence. |
| Godoy-Marín, H.; 2021(69) | Spain | Adenosine a2a receptors are upregulated in peripheral blood mononuclear cells from atrial fibrillation patients | Case-control | The study explores the expression of adenosine A2A receptor (A2AR) in right atrium biopsies and peripheral blood mononuclear cells from non-dilated sinus rhythm (ndSR), dilated sinus rhythm (dSR), and AF patients. | Samples from patients with sinus rhythms and atrial fibrillation were collected and analyzed using various methods, including gel electrophoresis, immunoblotting, RT-qPCR, cell culture, Flow Cytometry, and Confocal Imaging. | The study found increased A2AR expression in the right atrium of AF patients, with adenosine content and reduced ADA activity in plasma, and a positive correlation between A2AR expression and PBMCs. |
| Uma Mahesh R. Avula; 2021(70) | USA | Attenuating persistent sodium current–induced atrial myopathy and fibrillation by preventing mitochondrial oxidative stress | Experimental study | This study aims to comprehend the mechanisms influencing structural and electrophysiological remodeling in the atria due to an increased persistent sodium current. | The study involved crossbreeding mice expressing persistent sodium channels (NaV1.5 F1759A) with mice expressing human mitochondrial catalase (mCAT). | mCAT expression reduced mitochondrial oxidative stress, atria structural changes, atrial fibrillation, and ryanodine receptor dysfunction, reducing spontaneous and stimulation-induced atrial fibrillation. |
| Lin, P. H.; 2003 (72) | China | Oxidative damage to mitochondrial DNA in atrial muscle of patients with atrial fibrillation | Case-control | The authors utilized long-range polymerase chain reaction (PCR) to detect large-scale deletions of mtDNA in the atrial muscle of AF patients. | Right atrial appendages were removed from patients with chronic AF and sinus rhythm during heart surgery, and cellular DNA was extracted, revealing large-scale deletions. | The study found a high frequency of large-scale mtDNA deletions, particularly the 4977 bp deletion, in patients with atrial fibrillation (AF), with oxidative damage causing more significant damage. |
| Istratoaie, S.; 2022(73) | USA | Paraoxonase 1 and atrial fibrillation: Is there a relationship? | Case-control | The study aims to assess the concentration and activity of PON1 arylesterase (AREase) in patients with AF. | The study analyzed 67 patients with symptomatic paroxysmal or persistent AF admitted for cardioversion and 59 without AF, evaluating clinical parameters, lipid profile, PON1 concentration, and AREase. | Oxidative stress contributes to diseases like arrhythmias and increased risk of atrial fibrillation (AF), promoting endocardial dysfunction, left atrial thrombus, and stroke and influencing the efficacy of various drugs. |
| Samman Tahhan, A.2017[74] | USA | Association between oxidative stress and atrial fibrillation | Prospective study | The study hypothesized that prevalent and incident AF is associated with glutathione (EhGSH) and cysteine redox potentials, estimating systemic oxidative stress. | Aminothiol plasma levels in 1439 coronary angiography patients, including 148 with AF diagnoses, showed an 11.5% incidence of AF in 104 out of 917 patients after 6.3 years. | EhGSH levels in CAD patients increase the risk of prevalent and incident AF, independent of hsCRP level and other AF predictors, and correlate with CHA2DS2- VASc score. |

**AF:** Atrial Fibrillation**; EhGSH**: glutathione; **CAD**: Coronary Arterial Disease; **hsCRP**: high-sensitivity C-reactive protein; **PCR:** polymerase chain reaction**; PON1:** Paraoxonase 1**; OXPHOS** Mitochondrial Oxidative Phosphorylation; **eNOS:** endothelial Nitric Oxide Synthase**; ETC:** Electron Transport Chain; **O2:** oxygen; **NADPH:** Nicotinamide Adenine Dinucleotide Phosphate; **mtDNA:** mitochondrial DNA; **ROS:** Reactive Oxygen Species; **mCAT:** mitochondrial catalase; **ATP:** Adenosine Triphosphate; **RAS:** Renin-Angiotensin System; **EAT:** Epicardial Adipose Tissue; **8-OHdG:** 8-Hydroxy-2'-deoxyguanosine; **NOX:** NADPH oxidase; **SGLT:** sodium-Glucose Linked Transporter; **CAN:** Canagliflozin; **Gal-3:** galectin-3; **COS:** Costunolide; **XO:** xanthine oxidase; **WXKL:** Wenxin Keli; **DM:** diabetes mellitus; **Keap1:** Kelch-like ECH-Associating Protein 1; **Nrf2:** Nuclear factor erythroid 2-related factor 2; **NF-kB:** Nuclear Factor-kappa B; **LOX-1:** Lectin-like Oxidized Low-Density Lipoprotein Receptor-1; **ICAM-1:** Adhesion Molecule-1; **HO-1:** Heme Oxygenase-1;**ALS:** aliskiren; **TNF-α:** Tumor Necrosis Factor-alpha; **MCP1:** Monocyte Chemoattractant Protein-1**; VEGF:** Vascular Endothelial Growth Factor**; NTpBNP:** N-terminal pro-B-type**; iNOS:** inducible Nitric Oxide Synthase**; A2AR:** adenosine A2A receptor; **ndSR:** non-dilated sinus rhythm; **dSR:** dilated sinus rhythm.