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Review Article

Pharmacological Potentials of Omega 3 Fatty Acid in Reduction of Atrial Fibrillation

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Abstract

Atrial fibrillation (AF) is the most common type of arrhythmia in the general population with a prevalence that reaches one third of patients with arterial hypertension, diabetic and other risk factors. In atrial fibrillation, the regular impulses produced by the sinus node for a normal heart beat are overwhelmed by rapid electrical discharges produced in the atria and adjacent parts of the pulmonary veins. Omega-3 polyunsaturated fatty acids (PUFAs), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are permanent subjects of interest in relation to the protection of cardiovascular health and the prevention of the incidence of both ventricular and atrial arrhythmias. It has been proposed that Omega-3 polyunsaturated fatty acid possess anti-inflammatory properties that can inhibit arrhythmogenic mechanisms. Potential Targets of Omega-3 PUFAs Relevant to Arrhythmias Prevention are direct inhibition of sarcolemmal ion channels & restoring cardiac connexion channels. Intake of omega-3 fatty acids significantly prevents the occurrence of AF. The purpose of this review is to focus on the novel cellular and molecular effects of omega-3 PUFAs, in the context of the mechanisms and factors involved in the development of atrial fibrillation.

Keywords: Eicosapentaenoic acid, Docosahexaenoic acid, Atrial Fibrillation, Polyunsaturated fatty acids, Arrhythmias.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia encountered in the intensive care unit. Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, with a lifetime risk in the community of 25% and associated complications of heart failure, stroke and death.[1] As comorbidities of aging, pre-existing AF is common among patients presenting to the intensive care unit (ICU). As a frequent complication of critical illness, new-onset AF is also a problem familiar to ICU physicians.[2] Atrial fibrillation is the commonest sustained cardiac arrhythmia affecting approximately 33.5 million individuals worldwide.[1] In most patients, AF is also associated with an increased long-term risk of stroke.[3] The metabolic precursor of n-3 PUFA is the 18-carbon long chain with 3-double bonds alpha-linolenic acid (ALA). ALA can be found in vegetable oils, seeds, and nuts. The 20-carbon 5-double bonds eicosapentaenoic (EPA), the 22-carbon 5-double bonds docosapentaenoic (DPA), and the 22-carbon 6-double bonds docosahexaenoic acid (DHA) are synthesized from ALA through the action of desaturase and elongase enzymes.[4] Substantial amounts of EPA, DPA, and DHA can also be obtained by eating fish, fish oil, and other marine foods.[5] Dietary supplementation with v-3 PUFA reduces cardiovascular mortality and morbidity by affecting classic and emergent risk factors such as hypertension, hypertriglyceridemia, lipoprotein(a), and markers of inflammation, thrombosis and vascular reactivity.[6] Omega-3 polyunsaturated fatty acid, also commonly known as fish oil products, is concentrated sources of Eicosapentanoic acid and docosahexaenoic acid (DHA). It has been proposed that Omega-3 polyunsaturated fatty acid possess anti-inflammatory properties that can inhibit arrhythmogenic mechanisms.[7] Arrhythmogenic substrates, such as myocardial structural and ion channels remodeling, in the setting of inflammation and oxidative stress, facilitate occurrences of VF and AF as well.[8] Evidence suggests that omega−3 fatty acids modestly lower blood pressure (systolic and diastolic) in people with hypertension and in people with normal blood pressure.[9] Omega−3 fatty acids reduce blood triglyceride levels but do not significantly change the level of LDL cholesterol or HDL cholesterol in the blood.[10] In most patients, AF is also associated with an increased long-term risk of stroke.[11] New-onset postoperative atrial fibrillation (POAF) is a frequent complication of coronary artery bypass graft (CABG) surgery, with a reported incidence between11% and 40%.[12] It has been proposed that Omega-3 polyunsaturated fatty acid possess anti-inflammatory properties that can inhibit arrhythmogenic mechanisms.[13] Remodeling of atria into a proarrhythmic substrate is most often due to the development of atrial fibrosis.[14] Chronic heart failure, hypertension, valve disease, and myocardial infarction result in multiple, common pathways of inflammation, renin-angiotensin system activation, and generation of reactive oxygen species that produce atrial fibrosis.[15] AF may be initially triggered through multiple factors that perturb normal electrical conduction such as hypokalemia, hypomagnesemia, hypovolemia, and alterations in parasympathetic and sympathetic activity, leading atrial foci to develop abnormal automaticity, self-sustaining action potentials, or re-entrant circuits.[16] Bacteria can also alter calcium ion channel gene expression through toxin release,

resulting in a shortened atrial-effective refractory period which produces electrical remodeling that further predisposes to AF during sepsis.[17] Elevated inflammatory markers in patients with sepsis and postoperative patients are associated with an increased risk of developing AF.[18] Inflammation may predispose to arrhythmia development as a result of direct inflammatory cell infiltration and oxidative damage to atrial myocytes.[19] In the ICU, AF is more frequent among patients receiving vasopressor agents, in patients with electrolyte derangements, and in patients with greater disease severity.[19] Hypokalemia and changes in the balance of autonomic activity as a result of vasopressors may alter ion channel activity and cell automaticity that predispose to AF.[20] During AF, the coordinated depolarization and contraction of the heart is disrupted by innumerable, disorganized atrial electrical impulses leading to erratic contraction and loss of the "atrial kick" that assists with ventricular filling during diastole.[21] Atrial fibrillation is associated with a three-fold increased risk of incident heart failure (HF).[22] Hypertension, smoking, obesity, diabetes, renal impairment, sleep apnoea, and coronary artery disease are all associated with an increased risk of developing both HF and AF.[23] In HF, neurohormonal imbalance and activation of the renin–angiotensin–aldosterone system (RAAS) leads to maladaptive physiological changes including increased filling pressures and afterload. These can lead to increased left atrial stretch and fibrosis, contributing to the development of conduction abnormalities and facilitating the initiation and maintenance of AF.[24]

Atrial fibrillation is the commonest sustained cardiac arrhythmia affecting approximately 33.5 million individuals worldwide.[25] Women have a prolonged QT interval compared to men, on average by 10-20 ms.[26] The current evidence indicates that the overall prevalence of AF is in the range of 1% to 2% of the general population. The prevalence of AF continues to rise (41 cases per 1000 in 1993 to 85 cases per 1000 in 2007). It is estimated that between a quarter and two thirds of the AF population has transient or paroxysmal AF, which would not be accounted for in the early epidemiological studies based on populations with permanent AF diagnosed by electrocardiography.[27] The projected prevalence of AF in the United States in 2050, increases from 5.6 million (excluding paroxysmal and silent AF) to 12.1 to 15.9 million.[28] AF is the most common clinically important arrhythmia, with a recent worldwide estimate of up to 33.5 million patients (not even including those with clinically silent disease), and is increasing in prevalence, making this a global epidemic. The epidemiology of AF is more clearly established in Western developed countries than it is in developing nations.[29]

AF is characterized by findings including the presence of irregular R-R intervals and the absence of distinct P waves.[30] Mechanically, the chaotic electrical activity of AF leads to ineffective atrial contraction as well as further structural (and electrical) changes in the atria, which themselves potentiate AF.[31]Among competing theories, the "multiple wavelet hypothesis" proposes that there are multiple independent reentrant wavelets that exist within the fibrillating atria.[32]

ELECTROPHYSIOLOGY

There are multiple theories to explain the reason for atrial fibrillation. An important theory is that, in atrial fibrillation, the regular impulses produced by the sinus node for a normal heartbeat are overwhelmed by rapid electrical discharges produced in the atria and adjacent parts of the pulmonary veins. There are three fundamental components that favor the establishment of a leading circle or a rotor: slow conduction velocity of cardiac action potential, short refractory period, and small wavelength. Meanwhile, wavelength is the product of velocity and refractory period. If the action potential has fast conduction, with a long refractory period and/or conduction pathway shorter than the wavelength, an AF focus would not be established. In multiple wavelet theory, a wavefront will break into smaller daughter wavelets when encountering an obstacle, through a process called vortex shedding; but under proper conditions, such wavelets can reform and spin around a centre, forming an AF focus.[33]

ELECTROCARDIOGRAM

Atrial fibrillation is diagnosed on an electrocardiogram (ECG), an investigation performed routinely whenever an irregular heart beat is suspected. Characteristic findings are the absence of P waves, with disorganized electrical activity in their place, and irregular R–R intervals due to irregular conduction of impulses to the ventricles.[34] At very fast heart rates, atrial fibrillation may look more regular, which may make it more difficult to separate from other supraventricular tachycardias or ventricular tachycardia. QRS complexes should be narrow, signifying that they are initiated by normal conduction of atrial electrical activity through the intraventricular conduction system (Fig. 1). Wide QRS complexes are worrisome for ventricular tachycardia, although, in cases where there is a disease of the conduction system, wide complexes may be present in Afib with rapid ventricular response.[35]

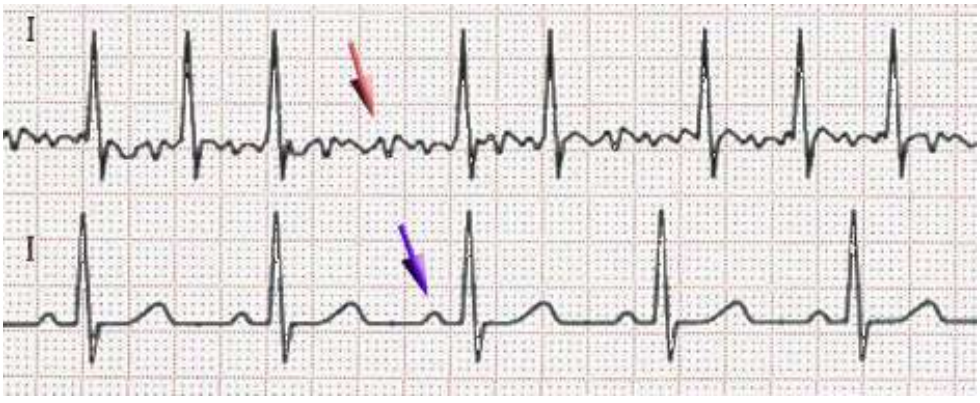

Figure 1: The figure shows ECG of atrial fibrillation (top) and normal sinus rhythm (bottom). The purple arrow indicates a P wave, which is lost in atrial fibrillation.[35]

RISKS FACTORS ASSOCIATED WITH ATRIAL FIBRILLATION

HYPERTENSION

Elevated blood pressure was the most important determinant, contributing to 20%–25% of all AF.[36] The mechanisms underlying this association relates to both haemodynamic alterations and activation of the renin-angiotensin-aldosterone system. The haemodynamic changes seen in association with obesity, hypertension causes increased ventricular after load and results in left ventricular hypertrophy, LA(Left atrial) enlargement and stiffness. The resultant diastolic dysfunction results in chronic LA stretch and dilation.[37] Hypertension increases the levels of circulating angiotensin II. Angiotensin II has also been shown to induce atrial fibrosis and hypertrophy, increasing the risk of electrophysiological changes associated with the development of AF (Fig. 2). Hypertension has been shown to be responsible for progression of atrial remodelling and the substrate therefore leading to AF.[38]

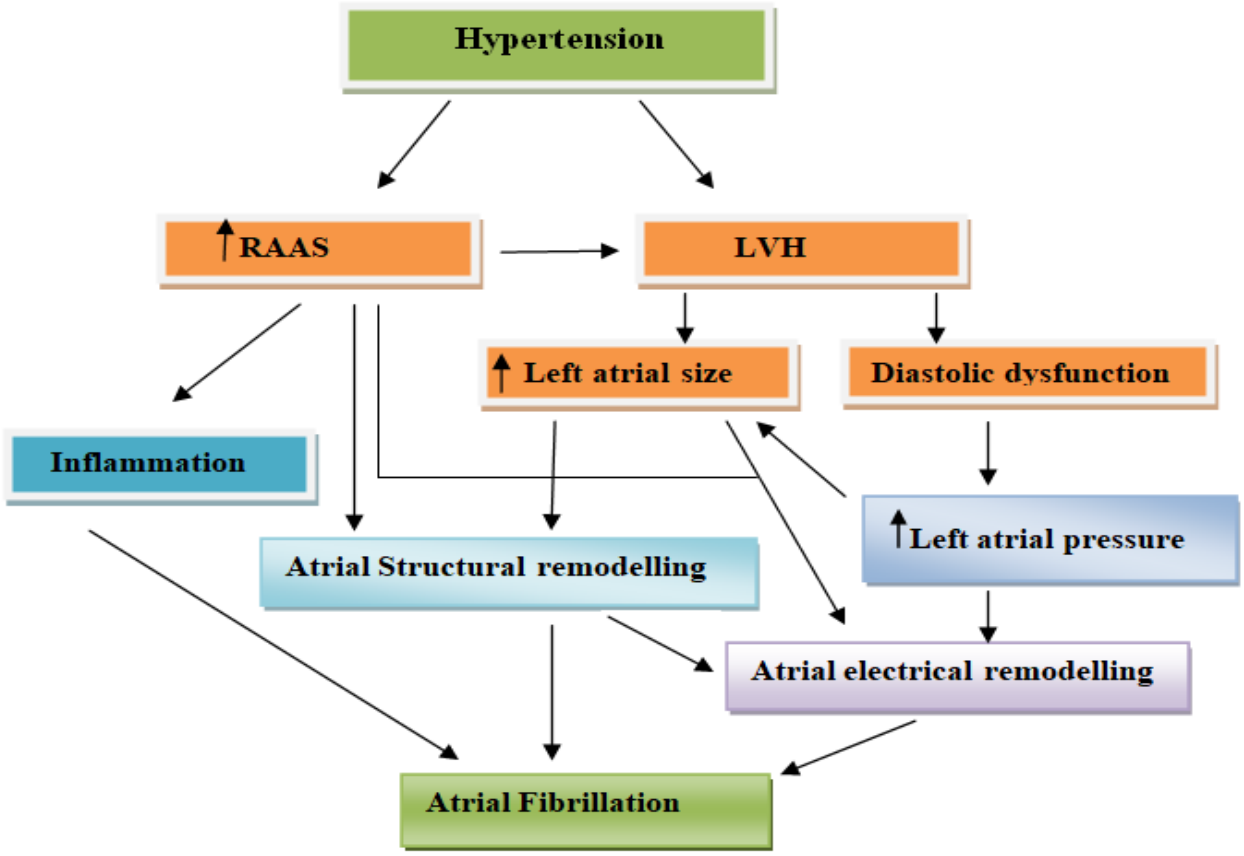

Figure 2: Role of Hypertension in Atrial fibrillation.[38]

AF ensues from multiple re-entry circuits that are initiated by firing of ectopic atrial foci on a vulnerable myocardial substrate. Refractoriness, slow conduction, and conduction barriers that perpetuate re-entry circuits leading to AF persistence characterize this substrate. Abnormalities of calcium handling are responsible for the ectopic foci, whereas structural and electric remodeling consisting respectively of atrial fibrosis and ion channel dysfunction underlies the vulnerable myocardial substrate.[39] Untreated or uncontrolled hypertension induces left ventricular hypertrophy; a condition associated with reduced ventricular compliance, increased ventricular wall stress, and decreased coronary flow reserve.[40]

OBESITY

Risk of incident AF has been shown to increase up to 29% with every 5-point increase in body mass index (BMI).[41] Significant weight loss is associated with a much reduced risk of incident AF development. Obese individuals have been demonstrated to have significantly increased left atrial (LA) pressure and volume and altered electro anatomic features in areas contiguous with pericardial fat. Obesity is also known to significantly alter circulatory haemodynamic, creating a high cardiac output state conducive to structural remodeling of the heart and results in an increase in the central blood volume as well as increased systemic vascular resistance which increases left ventricular wall stress causing hypertrophy and diastolic dysfunction.[42] This result in LA enlargement, which is known to be a potent independent predictor of AF. Pericardial fat volume which correlates with left atrial enlargement has been associated with increased risk of AF.[43]

DIABETES

Diabetes mellitus is another well-known cardiac risk factor. Fibrotic change within the atria in diabetes has been demonstrated in animals and humans, while electrical remodeling also appears to be an important mechanism for the association. Interstitial fibrosis is another prominent feature of atrial structural remodeling in diabetes. It involves the formation of collagen-rich myocardial tissue which also disrupts cell-to-cell coupling, hinders action potential propagation, and promotes reentrant excitation underlying fibrillatory activity.[44]

OBSTRUCTIVE SLEEP APONEA

Obstructive sleep apnoea (OSA) is a condition characterized by recurrent pharyngeal airway collapse leading to repetitive interruption of ventilation during sleep. Clinically, the condition presents with excessive daytime somnolence and treatment is with continuous positive airway pressure (CPAP).[45] Risk factors for the development of OSA are like those for AF and include obesity, hypertension, heart failure, ageing and upper airway soft tissue abnormalities.[46] Indeed, observational studies have suggested that OSA increases the risk of AF in a dose-dependent manner (increased severity OSA is associated with increased risk of AF). Risk of AF recurrence after cardioversion or AF ablation is significantly increased in patients with sleep apnoea.[47] The correlation of obstructive sleep apnea with cardiac dysfunction explained in Fig 3.

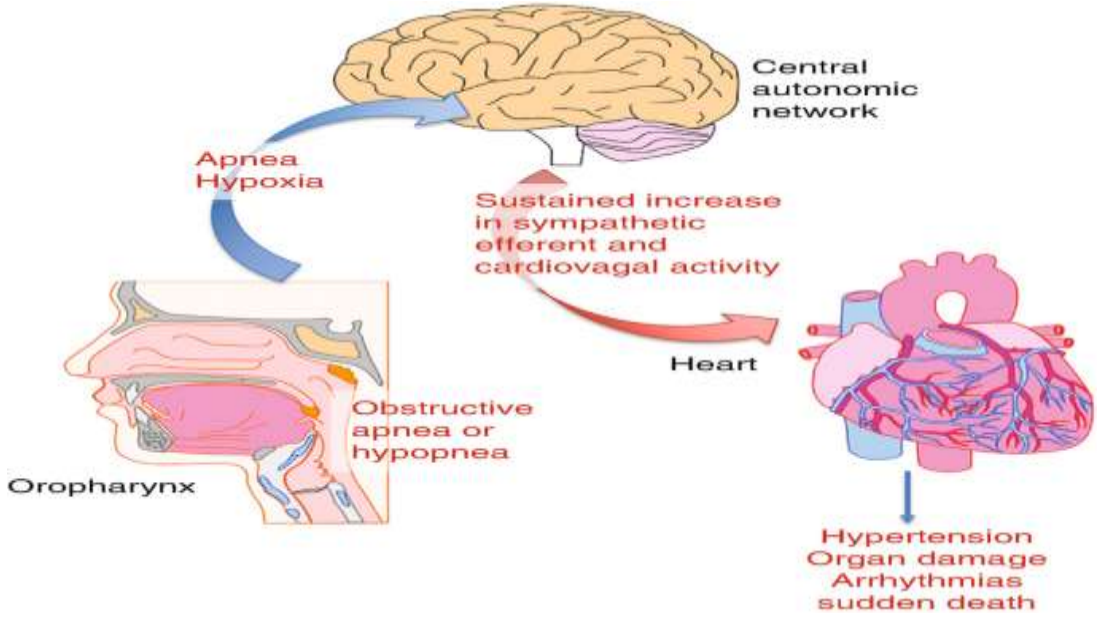

Figure 3: Correlation of obstructive sleep apnea with cardiac dysfunction.[47]

PHYSICAL INACTIVITY

Physical activity has been widely reported to reduce cardiovascular disease incidence. Compared with sedentary, runners had a significantly reduced risk of 30% and 45% of all-cause and cardiovascular mortality, respectively. Physical inactivity is known to promote obesity.[48] It has been shown that early inactivity leads to subsequent obesity. Independent of obesity, physical activity predicts a lower risk of cardiovascular disease. Specifically for AF, greater levels of physical activity result in lowered incidence of AF.[49]

ROLE OF CARDIAC HYPOXIA IN ATRIAL FIBRILLATION

Structural changes such as cardiac fibrosis are among the risk factors leading to the development of AF Once atrial fibrosis is established, it is irreversible and contributes to sustaining AF possibly by impairing atrial conduction and promoting atrial anisotropy, thus favoring atrial micro-reentry.[50] A deficient oxygen supply is often a cause of myocardial dysfunction. This can result in cardiac remodeling and fibrogenesis, which may cause, among other things, heart failure on the ventricular level and dysrhythmias like AF, which is promoted by selective atrial ischemia.[51] Cardiac remodeling and fibrogenesis may impair coronary microcirculation. Thus, cardiac fibrosis could possibly increase oxygen diffusion distances from capillaries to myocytes by accumulation of myocyte-encircling collagen in the interstitium.[52] This would permit local hypoxia and could alter angiogenesis and trigger cellular adaptation. The hypoxia-inducible factor (HIF) pathway has been implicated in AF development. HIF1 is a heterodimer consisting of HIF1α and HIF1β. Oxygen promotes the hydroxylation of HIF1, a required condition for von Hippel–Lindau protein to associate with and inactivate HIF1.[53] In the absence of oxygen, however, HIF1 binds to the hypoxia response elements and, thus, induces genes such as the vascular endothelial growth factor (VEGF) VEGF may interact with various receptors, among which the kinase insert-domain containing receptor KDR (VEGF receptor 2) is the key receptor for the transmission of its angiogenic effects.[54] Once activated through phosphorylation (pKDR), it results in mitogenic, chemotactic, and prosurvival signals transmitted by proteins like the platelet-derived growth factor (PDGF), carboanhydrase IX, and the apoptosis-inhibiting protooncogene B-cell lymphoma 2 (Bcl-2) proteins (Fig 4). Furthermore, in hypoxia, endoglin (CD105) is up-regulated. CD105, a 180-kDa homodimeric proliferation-associated glycoprotein, is abundantly expressed in angiogenic endothelial cells. It has a strong homology to the transforming growth factor (TGF)-β receptor type III (TβRIII) and promotes (profibrotic) TGF-β binding to its type I and type II receptors (TβRI and TβRII) and, thus, extracellular matrix formation. CD34, also a glycoprotein, is expressed on endothelial cells and functions as a marker of microvessel density (MVD).[55]

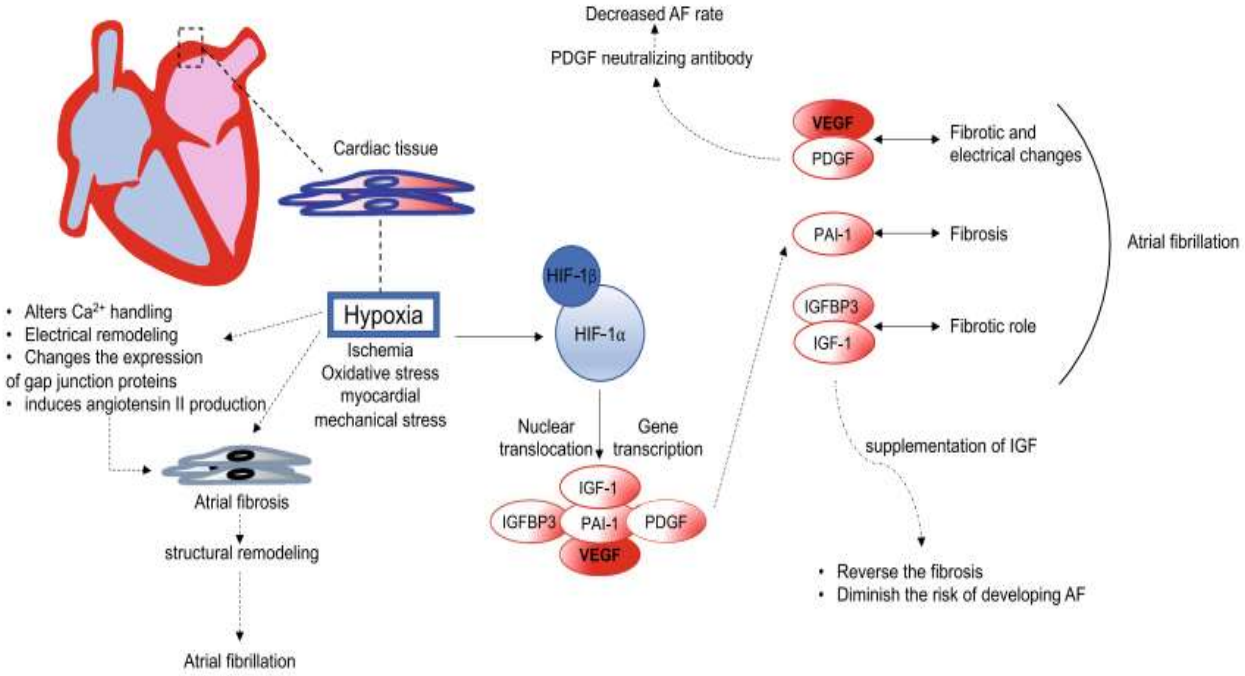

Figure 4: Schematic demonstrating the role of hypoxia-inducible factor-1 and its related cytokines in atrial fibrillation. HIF hypoxia inducible factor; IGF-1 insulin-like growth factor-1; IGFBP-3 insulin like growth factor binding protein-3; PAI-1 plasminogen activator inhibitor-1; PDGF platelet-derived growth factor; VEGF vascular endothelial growth factor.[55]

ROLE OF MYELOPEROXIDASE (MPO) IN ATRIAL FIBRILLATION

Myeloperoxidase (MPO), secreted by neutrophils under inflammatory conditions, is elevated in atrial fibrillation (AF).[56] MPO may be involved in atrial remodeling that underpins AF progression characterized by a switch from paroxysmal to persistent AF and the formation of low-voltage areas (LVA). MPO levels are modulated by renin–angiotensin system antagonists (RAS-A), commonly used to treat AF co-morbidities, and are associated with reduced AF incidence.[57] Under physiological conditions, MPO is best known for its antibacterial properties characterized by the formation of reactive oxygen species which oxidize, and thus destroy bacterial cell walls. In AF, however, these reactive oxygen species may contribute to the activation of matrix metalloproteinases which in turn generate a pro-fibrotic environment.[58] MPO release from activated immune cells initiates fibrotic remodeling by activating matrix metalloproteinases which in turn modulate the extra-cellular matrix resulting in myofibroblast activation and the vicious cycle of fibrosis. RAS-A impair Angiotensin II signaling, which was found to promote neutrophils activation, and therefore release of MPO.[59] Inflammation induced by atrial fibrillation shown in Fig 5.

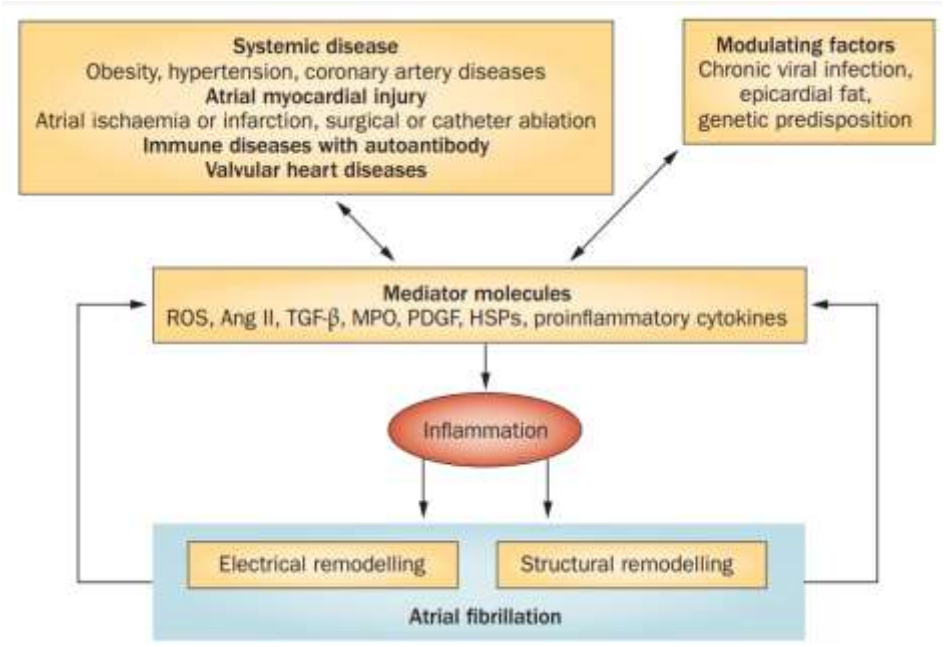

Figure 5: Activated inflammatory pathways alter the electrophysiology, structure, and autonomic remodelling of the atria. Inflammation induced by atrial fibrillation can establish an inflammatory cycle that leads to increased severity of the arrhythmia.
Abbreviations: Ang II, angiotensin II; HSP, heat shock protein; MPO, myeloperoxidase; PDGF, platelet-derived growth factor; ROS, reactive oxygen species; TGF-β, transforming growth factor β.[60]

ROLE OF COPD IN ATRIAL FIBRILLATION

Chronic obstructive pulmonary disease (COPD) is independently associated with atrial fibrillation.[61] Decreased oxygenation, hypercapnia, pulmonary hypertension, diastolic dysfunction, oxidative stress, inflammation, changes in atrial size by altered respiratory physiology, increased arrhythmogenicity from nonpulmonary vein foci commonly located in the right atrium, and respiratory drugs have been implicated in the pathogenesis of AF in COPD. Hypoxia-induced vascular endothelial growth factor (VEGF) expression is strongly regulated by hypoxia-inducible factor-1a (HIF-1a), the transcriptional factor for VEGF, which is a critical modulator for sensing and responding to changes in the oxygen concentration. MMP-9 expression increases in fibrillating atria, and may contribute to atrial structural remodeling of AF.[60]

HIF-1a promotes the expression of TGF-b1 and MMP-9 protein, and thus is involved in atrial fibrosis. Prolonged QT interval corrected by using the Framingham formula (QTc) as a predictor of incident AF, and showed that prolonged QTc predicts a roughly 2-fold increased risk of AF. QTc interval reflects the atrial effective refractory period (AERP), suggesting that QTc interval may be used as a marker of atrial refractoriness relevant to assessing AF.[62] COPD induced AF explained in Fig 6.

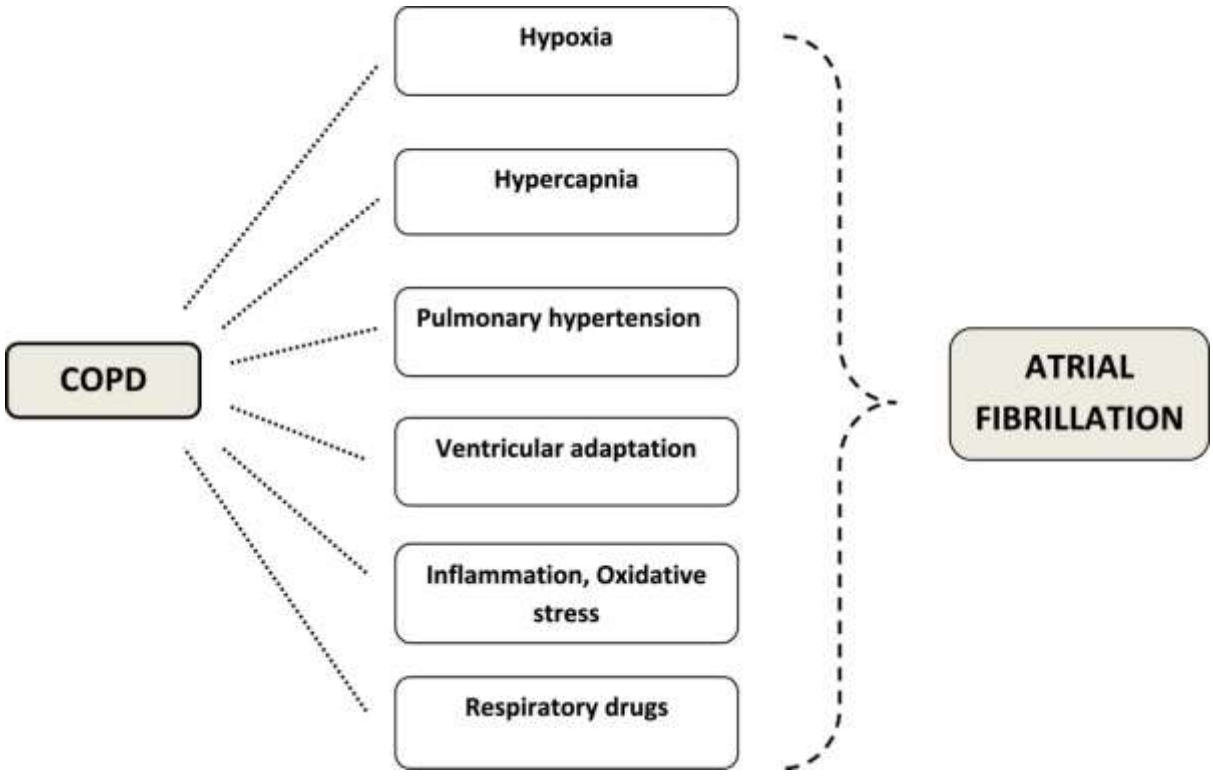

Figure 6: Independent association of COPD with atrial fibrillation.[62]

ROLE OF HYPERCAPNIA IN ATRIAL FIBRILLATION

Hypercapnia has also been implicated in AF occurrence in COPD. Hypercapnia produces a marked and uniform increase in atrial refractoriness and a significant slowing in atrial conduction. Return of CO2 to normal results in rapid return of refractoriness to baseline levels but conduction slowing persists, suggesting that hypercapnia may create the substrate for AF after correction.[53] Hypercapnia and hypoxemia produce pulmonary arteriolar constriction leading to pulmonary arterial and right ventricular hypertension. Right ventricular hypertension may induce arrhythmias by leading to right atrial dilatation and increasing transmural pressure on endocardial vessels altering the distribution of blood flow. In COPD exacerbations, AF is more frequent with higher levels of PaCO2 and higher values of pulmonary artery systolic pressure.[63]

ROLE OF POTASSIUM IN ATRIAL FIBRILLATION

Serum potassium, especially hypokalemia (>3.5 mmol/l), is suggested to be associated with a higher risk of cardiovascular disease, especially ventricular arrhythmias and cardiac arrest. Few studies previously investigated the association of serum potassium with the risk of atrial fibrillation.[64] lower serum potassium levels were associated with a higher perioperative risk of atrial fibrillation (Fig 7). Haemodialysis patients found low serum potassium to be associated with an increase in P-wave duration, a marker of atrial conduction. P-wave duration increase has been associated with a higher risk of atrial fibrillation. The most likely mechanism through which serum potassium leads to an increased risk of atrial fibrillation is by the influence of potassium on the cell membrane potential.[65] It is proposed that a low serum potassium level causes cellular hyperpolarity, increases resting potential and hastens depolarization.[66]

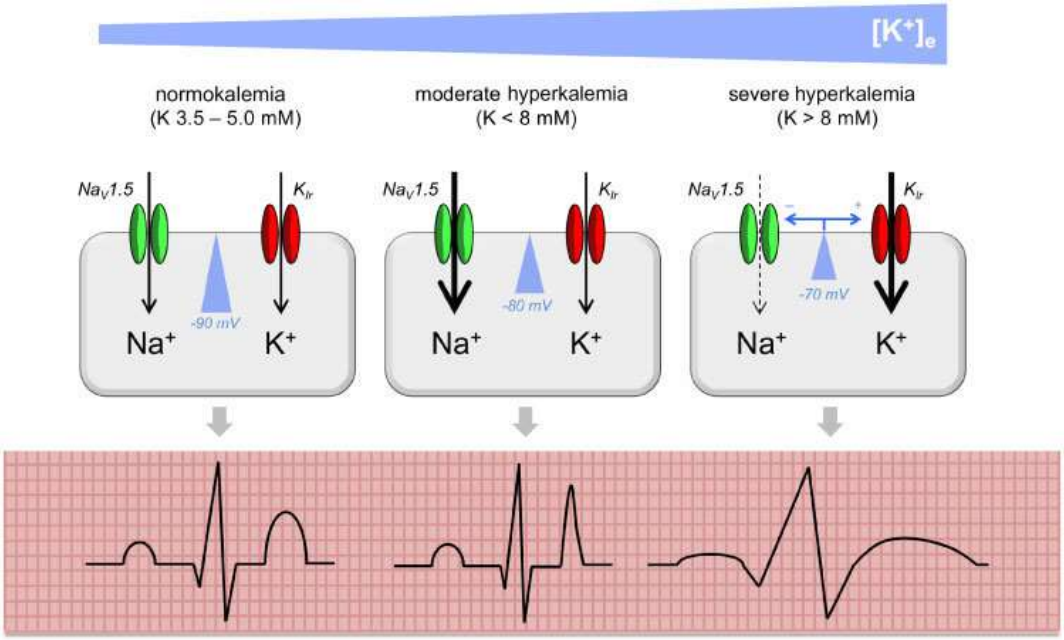

Figure 7: Mechanism of cardiac arrhythmia in hyperkalemia. In normokalemia, the cell membrane of the cardiomyocyte is polarized (resting potential around À90 mV). In moderate hyperkalemia, the cell membrane becomes partially depolarized, bringing the resting potential closer to the threshold potential for AP initiation. Therefore fast sodium channels (Na v 1.5) are activated more readily, increasing excitability and conduction velocity. These manifests as T wave peaking on the ECG as a mass of ventricular cardiomyocytes undergo (synchronous) early repolarization. In severe hyperkalemia, voltage-dependent inactivation of Na v 1.5 channels and activation of inwardly rectifying potassium channels (K ir) lead to reductions in conduction velocity and can render cells refractory to excitation. This manifests as broadening of ECG complexes and/or conduction blocks. This figure represents an idealized model, as there is poor correlation between ECG features and the degree of hyperkalemia.[66]

ROLE OF PLASMA TROPONIN IN ATRIAL FIBRILLATION

Cardiac troponin is a marker for myocardial damage in patients undergoing CABG or patients with myocardial infarction.[67] The peak value reflects the extent of myocardial damage and postoperative elevation is a predictor of adverse outcome (myocardial infarction, shock and mortality) Furthermore, increased preoperative cardiac troponin was found to be associated with morbidity and mortality.[68] Although the Pathophysiology of AF after CABG is multifactorial, perioperative systemic inflammation plays an important role. The extent of myocardial damage, reflected by the degree of postoperative myocardial enzyme elevation, may be associated with the development of AF as well; more extensive surgery might lead to oedema and myocardial cell decay, further interrupting electrical impulses and increasing the risk of developing an irregular rhythm (Fig 8).[69]

The value of perioperative cardiac enzyme assessment for the prediction of AF has been investigated earlier.[70] They found that patients with postoperative AF had significantly higher cTNT values. Perioperative N-terminal pro-B-type natriuretic peptide was also an independent risk factor for the prediction of AF after oesophageal and thoracic surgery both pre- and postoperatively.[71]

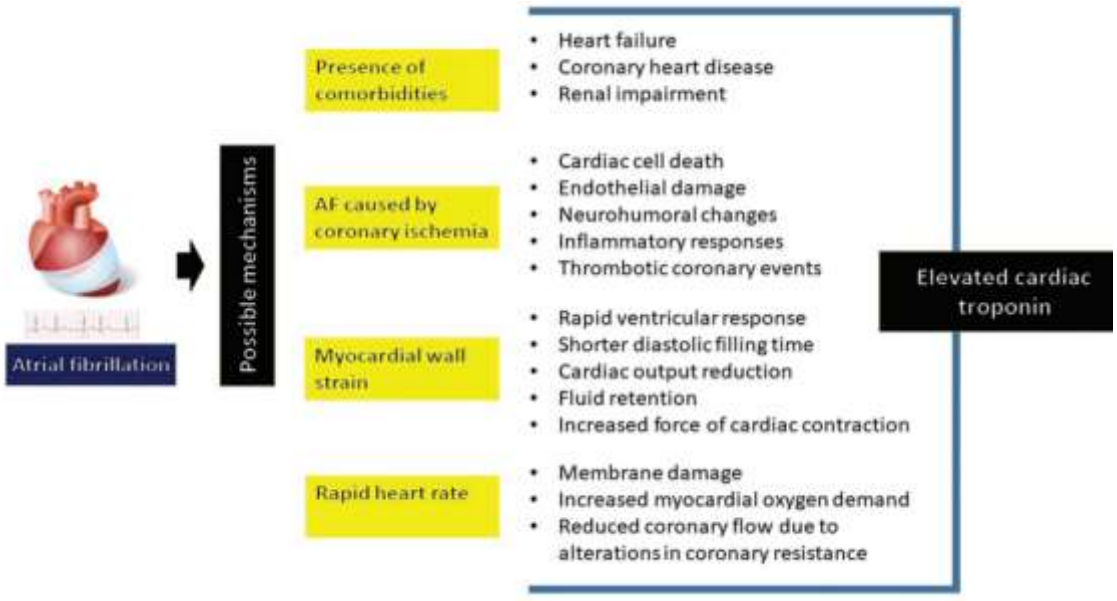

Figure 8: Possible mechanisms through which atrial fibrillation may lead to elevated cardiac troponin.[71]

OMEGA-3 POLYUNSATURATED FATTY ACIDS

Omega-3 polyunsaturated fatty acids (PUFAs), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are permanent subjects of interest in relation to the protection of cardiovascular health and the prevention of the incidence of both ventricular and atrial arrhythmias. The efficacy of omega-3 PUFA intake is manifested more obviously in the prevention and treatment of coronary heart disease (CHD) than in the prevention or treatment of life-threatening arrhythmias.

POTENTIAL TARGETS OF OMEGA-3 PUFAs RELEVANT TO ARRHYTHMIAS PREVENTION

The anti-arrhythmic effects may be attributed to omega-3 PUFAs include direct and indirect modulation of ion channel properties, membrane composition and fluidity as well as anti-inflammatory and anti-fibrotic effects and modulation of sympatho-vagal balance.

The antiarrhythmic effect attributed to omega-3 PUFAs include direct and indirect modulation of:

- Direct inhibition of sarcolemmal ion channels.[72] (Na, Ca and K currents)
- Modulation of sympatho-vagal balance.[73]
- Modulation of ion channels properties.[74]
- Membrane composition and fluidity.
- Inhibition of sarcoplasmic reticulum RyR channels.
- Prevention of calcium overload and oxidative stress.
- Inhibit up-regulation of sodium hydrogen antiporter 1 activity.
- By restoring cardiac (connexin) Cx43 channels.

ANTI-ARTERIOSCLEROTIC EFFECT OF OMEGA-3 POLY UNSATURATED FATTY ACID

Increased production of nitric oxide through the consumption of omega-3 PUFA may increase the expression of endothelial nitric oxide synthase. Intake of omega-3 PUFA improves the serum markers of endothelial dysfunction, such as E-selectin, VCAM-1, and ICAM-1. Intake of omega-3 PUFA improves flow-mediated vasodilation, among other parameters of endothelial function.[75] Omega-3 PUFA have been reported to reduce serum triglycerides in patients with hypertriglyceridemia and an increase in LDL-C and HDL-C can accompany a reduction in triglycerides. The increase in LDL-C is less than the reduction in VLDL-C, resulting in a net decrease in non-HDL-C (VLDL-C plus LDL-C). The administration of high- purity EPA reduces CVD risk by approximately 19%.[76]

CONCLUSION

In this review, it may be concluded that omega-3 fatty acids significantly produces marked effects in prevention of atrial fibrillation. Omega-3 polyunsaturated fatty acids possess anti-inflammatory properties that can inhibit arrhythmogenic mechanisms. It can reduce blood triglyceride levels but do not significantly change the level of LDL cholesterol or HDL cholesterol in the blood. The factors which are responsible for AF was decrease in the Hb level, increase in plasma troponin and decrease in potassium levels which are markedly treated by EPA & DHA supplements. Omega-3 PUFAs cause direct and indirect modulation of ion channel properties and sympatho-vagal balance. Although it will increase the Hb level of blood and decrease the hypercapnia and plasma troponin level which are the potent marker of arrhythmogenic substrate. Association of serum potassium with the risk of atrial fibrillation can markedly reduced by omega-3 polyunsaturated fatty acids. Thus our investigation indicates that omega-3 fatty acids involved in cardio protective effects of arrhythmias like atrial fibrillation.

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