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Abstract: Atrial fibrillation (AF), a complex cardiac arrhythmia, necessitates a shift in management paradigms, emphasizing an integrative approach that incorporates lifestyle modifications. Investigations into the role of interleukins and inflammatory mediators are underway, exploring their potential as diagnostic markers and predictors of cardiovascular events in AF. Despite the identification of biomarkers related to cardiac remodeling, their predictive ability for post-cardioversion outcomes remains controversial. Computational models are being developed to understand proarrhythmic contributions and identify anti-AF targets. Addressing the rising global incidence of AF, linked to stroke and heart failure, presents a critical health challenge. As risk factors like obesity prevail, AF becomes a pervasive public health concern, expected to double in prevalence over the next 50 years. The impact on mortality and morbidity, especially through hospitalizations, underscores the need for early detection and effective clinical management. Identifying individuals at increased AF risk becomes crucial for screening and prevention strategies. Lifestyle modifications, including weight management and physical activity, emerge as influential factors in AF management, offering the potential to alleviate symptoms and modify disease progression. The paper concludes by emphasizing the need for safer antiarrhythmic therapies based on AF mechanisms, promising improvement in global AF management. The multifaceted nature of AF etiology requires a broader perspective beyond traditional medical interventions, acknowledging the importance of integrated care to address this significant public health chall.

Keywords: atrial fibrillation; inflammatory mediators; biomarkers; global health challenge; lifestyle modifications; cardiovascular outcomes; antiarrhythmic therapies

Introduction

Atrial fibrillation (AF) is a complex cardiac arrhythmia associated with adverse cardiovascular outcomes. Traditional management paradigms are being reevaluated to include lifestyle modifications due to their significant impact on AF trajectory [1]. The focus on pharmacological and procedural interventions is shifting towards a more integrative approach [2]. The role of interleukins and inflammatory mediators in the pathogenesis, prognosis, and treatment of AF is being investigated, with potential for their use as markers of diagnosis and cardiovascular events [3]. Biomarkers related to cardiac remodeling, fibrosis, inflammation, oxidative stress, and adipose tissue dysfunction have been identified, but their predictive ability for post-cardioversion outcomes is still controversial [4]. Computational models are being developed to understand the proarrhythmic contributions of AF-induced alterations and identify novel anti-AF targets [5]. In addition, targeting inflammatory signaling and fibroblast function may prevent structural remodeling and progression of AF. The development of more effective and safer antiarrhythmic therapies based on the underlying mechanisms of AF is a promising avenue for improving AF management.

A Global Health Challenge:

The increasing incidence of atrial fibrillation (AF) is a global health challenge due to its links to stroke, heart failure, and cardiovascular morbidity. As societies age and risk factors like obesity and sedentary lifestyles become more prevalent, AF has become a pervasive public health concern. The multifaceted nature of AF etiology requires a broader perspective beyond traditional medical interventions [6–8]. The prevalence of AF is expected to more than double over the next 50 years, leading to significant clinical implications and healthcare cost burden [9]. AF is associated with increased mortality and morbidity, particularly due to hospitalizations [10]. Early detection and characterization of AF patients are crucial for effective clinical evaluation and management. The identification of individuals at increased risk of AF can aid in screening, surveillance, management, and prevention strategies. The care burden of AF and its consequences impact health systems, emphasizing the need for thromboembolic prophylaxis and integrated AF care.

Shifting Perspectives: Lifestyle Modifications in AF Management:

Lifestyle modifications have emerged as pivotal influencers in AF management, with the potential to alleviate symptoms and modify the course of AF development. Weight management, physical activity, dietary choices, and risk factor reduction have all been shown to play a role in AF management [11]. This shift in perspective challenges traditional dogmas and encourages a more nuanced understanding of AF pathogenesis [12]. Contemporary research has highlighted the intricate interplay of genetic, inflammatory, and lifestyle factors in shaping the course of AF [13]. By addressing lifestyle factors, such as weight, physical activity, and diet, clinicians can potentially improve AF outcomes and reduce the burden of the condition [14]. Lifestyle modifications offer a complementary approach to pharmaceutical and procedural solutions, providing patients with additional tools to manage their AF effectively [15].

Objective of the Review: Synthesizing the Impact of Lifestyle Changes on AF:

Lifestyle changes play a significant role in the management of atrial fibrillation (AF) [11,13]. Patients with AF can benefit from virtual education programs that provide knowledge, skills, and self-efficacy, while reducing anxiety and normalizing their experience [15]. Additionally, lifestyle modifications such as adaptive foraging (AF) by consumers can enhance community stability and promote further diversification of niche traits [16]. In Africa, there is a high prevalence of overweight and obesity among patients with type 2 diabetes, highlighting the need for innovative weight management interventions tailored to the cultural context [17]. Older adults in China's Yangtze River Delta region exhibit a stronger preference for aging in place (AIP) in more developed cities, with individual characteristics, mental health, and physical health influencing AIP preference. Overall, lifestyle changes have the potential to positively impact AF management, community stability, weight management in type 2 diabetes, and aging in place preferences [17].

II. The Multifaceted Etiology of AF

Traditional Approaches: Comprehensive Exploration of Pharmacological and Procedural Interventions in AF Management

Traditional therapeutic strategies for Atrial Fibrillation (AF) have primarily centered around pharmacological agents and procedural interventions. In this section, we embark on a thorough examination of these conventional approaches, acknowledging their historical significance while critically assessing their limitations in addressing the nuanced and multifaceted nature of AF etiology.

Pharmacological Interventions:

Pharmacological interventions for atrial fibrillation (AF) have historically focused on restoring and maintaining normal sinus rhythm. However, these antiarrhythmic medications are limited by the risk of proarrhythmia, potential side effects, and variable individual responses. The challenges associated with pharmacological rhythm control have highlighted the need for alternative strategies that go beyond traditional drug-based interventions [18–20].

Procedural Interventions:

Procedures like catheter ablation have gained prominence in managing AF, targeting arrhythmogenic foci within the heart. While ablation has shown success in certain cases, its efficacy

can be variable, and the invasiveness of the procedure poses inherent risks [21]. Moreover, not all patients are suitable candidates for these interventions, emphasizing the necessity for a more comprehensive understanding of AF etiology to guide treatment decisions [22]. There is growing evidence that catheter ablation may reduce HFpEF severity, hospitalization, and mortality compared to medical management [23]. Individualized ablation strategies stratified by stepwise substrate inducibility provide a logical basis for catheter-based rhythm control in this heterogeneous population [24]

III. Beyond Electrophysiology: Evolving Perspectives on AF Etiology

A holistic understanding of atrial fibrillation (AF) etiology requires considering factors beyond electrophysiology. Genetic predisposition, inflammatory processes, and lifestyle factors all play a role in shaping the trajectory of AF [25–28]. Electrophysiological abnormalities alone may not provide a complete picture of AF etiology, and a comprehensive approach is needed to unravel the complex interplay between these factors. Genetic studies have identified mutations associated with AF, highlighting the importance of genetic predisposition [29]. Inflammatory processes, such as atrial fibrosis, have been linked to AF and can be assessed through echocardiography. Lifestyle factors, including diet, exercise, and stress, also contribute to AF development. By considering these multifaceted aspects, a deeper understanding of AF etiology can be achieved, leading to improved prevention and management strategies.

Genetic Factors:

Familial forms of atrial fibrillation (AF) have been identified, and genetic loci associated with AF have been mapped. Family history of AF is associated with an increased risk of first-degree relatives developing AF. Mutations in potassium channel genes (ABCC9, HCN4, KCNA5, KCND3, KCNE1, KCNE2, KCNE3, KCNE4, KCNE5, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNN3, and KCNQ1) and sodium channel genes (SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, and SCN10A) have been identified as causing AF. Gain-of-function mutations increase repolarizing K+ current, while loss-of-function mutations delay repolarization and promote Ca2+ mediated afterdepolarization. Other genetic variants, such as mutations in the GJA5 gene, affect cell-cell coupling and conduction velocity. Genome-wide association studies have identified genetic variants associated with AF susceptibility, including SNPs on chromosomes 4q25 and 16q22. The Pitx2 gene, involved in embryonic organogenesis, and the ZFHX3 gene, involved in Ca2+ regulation, have also been implicated in AF. The AFGen consortium has identified 17 independent susceptibility signals for AF at 14 genomic regions. These findings may lead to the assessment of individual AF risk and the discovery of new therapeutic targets [30–32].

Inflammatory Pathways:

Inflammatory pathways play a role in triggering AF and AF, in turn, increases the inflammatory state. Elevated levels of inflammatory biomarkers, such as CD40 ligand, fibrinogen, matrix metalloproteinase-9 (MMP-9), and C-reactive protein, have been observed in patients with AF. Inflammation leads to electrical and structural remodeling of the atria, promoting the maintenance and occurrence of AF. Inflammatory markers, including the systemic immune inflammation index, neutrophil-lymphocyte ratio, and platelet/lymphocyte ratio, have been found to be higher in patients with AF compared to those with normal sinus rhythm [33]. Inflammation triggers AF by amplifying inflammatory pathways, leading to atrial structural remodeling, atrial dilatation, and increased fibrosis in the atrial myocardium. This inflammatory state also causes downregulation of potassium channels and calcium handling-associated genes, as well as decreased expression of connexin 40, resulting in arrhythmogenic electrical remodeling. Additionally, inflammation promotes autonomic remodeling by upregulating sympathetic and parasympathetic innervation and neurotrophin expression in the atria. The interaction between inflammation and AF forms a vicious cycle, where AF further increases the inflammatory state [34–37].

VI. Integration of Lifestyle Factors: Recognizing Lifestyle as Integral to AF Pathogenesis

Lifestyle factors, including dietary habits, physical activity levels, cardiovascular health, and BMI, have been recognized as modifiable determinants that influence the development and progression of atrial fibrillation (AF) [13,38]. These lifestyle choices play an integral role in the

intricate web of AF pathogenesis, extending beyond genetic and electrophysiological factors [39]. There is increasing interest in understanding and measuring behavioral risk factors associated with AF, such as alcohol consumption, sedentariness, and smoking, in order to reduce stroke risk [40]. Studies have shown that lifestyle interventions, emphasizing physical activity, weight loss, and adherence to a Mediterranean diet, can have a favorable effect on blood concentrations of biomarkers related to AF pathways, such as high-sensitivity C reactive protein (hsCRP), 3-nitrotyrosine (3-NT), and N-terminal propeptide of B-type natriuretic peptide (NT-proBNP) [33]. These findings highlight the importance of considering lifestyle factors in the prevention and management of AF.

Dietary Influences:

One study found that adherence to Mediterranean-style or Dietary Approaches to Stop Hypertension (DASH) diets was associated with a lower incidence of AF, but these associations were no longer significant after accounting for lifestyle factors, with obesity being a major factor [41]. Another study failed to show an association between specific dietary patterns, including the Mediterranean diet, and AF development [42]. Reducing the consumption of ultra-processed foods may be important for the primary prevention of atrial fibrillation (AF) [41]. However, a Mendelian randomization study found a significant correlation between high dietary salt intake and increased risk of AF. The study found that the odds ratio for AF per unit increase in dietary salt intake was 1.36 (95% CI, 1.04-1.77) [43]. Let's delve into the contrasting findings and the implications of these studies:

Mediterranean-Style or DASH Diets and AF Incidence:

Positive Associations: A study proposed that following Mediterranean-style or Dietary Approaches to Stop Hypertension (DASH) diets was linked to a reduced occurrence of atrial fibrillation (AF). These dietary patterns emphasize the consumption of fruits, vegetables, whole grains, and lean proteins, which are believed to confer cardiovascular benefits. Additionally, the identification of Indo-Mediterranean and Japanese foods, such as pulses, porridge, spices, millets, guava, blackberry, soya tofu, whole rice, vegetables, and fish rich in fish oil, fish peptides, and taurine, has been associated with lower blood pressur [41,43,44].

Mixed Findings on Specific Dietary Patterns:

Role of Ultra-Processed Foods:

Highly processed foods often contain high levels of salt, unhealthy fats, and additives, which can contribute to inflammation, oxidative stress, and other factors associated with AF [41]. The excessive intake of ultra-processed foods can lead to imbalanced diets, obesity, and metabolic disorders [45]. Studies have shown a strong association between the consumption of ultra-processed foods and an increased risk of developing chronic conditions such as type 2 diabetes and certain types of cancers [46]. Additionally, the non-nutritional properties of ultra-processed foods, such as their high palatability and rewarding stimulus, can influence feeding facilitation and eating behavior [47].

Dietary Salt Intake and Mendelian Randomization:

Contradictory Findings:

A Mendelian randomization study found a significant correlation between high dietary salt intake and an increased risk of AF [43]. This contradicts previous studies and suggests that the impact of dietary salt on AF may be more nuanced than initially thought. The study used genetic instruments for dietary salt intake from a genome-wide association study and summary-level data for AF from another GWAS. Multiple MR methods were employed, including the IVW method, MR-RAPS, maximum likelihood estimation, and MR-PRESSO. All methods consistently showed a significant correlation between dietary salt intake and the risk of AF. These findings provide robust evidence supporting the association between dietary salt intake and AF risk. However, further research is needed to clarify this relationship and translate the findings into clinical practice [48].

Consideration of Genetic Factors:

Mendelian randomization studies provide evidence that individuals genetically predisposed to high salt intake may have an elevated risk of atrial fibrillation (AF) [43]. This highlights the importance of considering genetic factors when examining the relationship between diet and AF. Additionally, Mendelian randomization has been used to investigate the potential causalities of polyunsaturated fatty acids (PUFAs) with sepsis and mortality risk [49]. The use of genetic variants

as instrumental variables in Mendelian randomization studies allows for a more robust assessment of causality, overcoming biases present in observational studies [50]. Furthermore, Mendelian randomization has been applied to assess the causal effects of various clinical factors on coronary artery disease (CAD) [51]. These studies have identified causal effects of cardiometabolic traits and other clinical factors on CAD, emphasizing the importance of considering genetic factors in understanding disease etiology [52].

In summary, the relationship between diet and atrial fibrillation is multifaceted and influenced by various factors, including lifestyle, obesity, and genetic predispositions. While certain dietary patterns, such as the Mediterranean or DASH diets, may initially appear beneficial, the complexity of the interplay with lifestyle factors complicates the interpretation of findings. The contradictory results on salt intake further emphasize the need for a nuanced understanding of the role of specific dietary components in AF development.

Physical Activity and AF:

The impact of physical activity on AF risk and progression is multifaceted. Regular physical activity and exercise training are integral for the secondary prevention of cardiovascular disease, including AF. Moderate-intensity exercise and remaining physically active are recommended to prevent AF incidence or recurrence [53]. A proposed evidence-based recommendation for patients with AF is 360-720 MET-minutes/week, corresponding to approximately 60-120 minutes of exercise per week at moderate-to-vigorous intensity [54]. Non-traditional, low-moderate intensity exercise, such as Yoga, may also have promising benefits on patient quality of life and physical capacity [46]. Short-term exercise-induced cardioprotection and 'non-response' to exercise training are interesting concepts in AF rehabilitation [55]. Excessive endurance exercise may paradoxically increase the risk of AF, highlighting the need for a balanced approach to exercise and AF risk reduction.

Let's explore the multifaceted impact of physical activity on AF risk and progression, taking into consideration different intensities, types of exercise, and potential nuances:

Regular Physical Activity and Secondary Prevention:

Cardiovascular Benefits:

The quantity of visceral fat that is accumulated in the body can be reduced by frequent exercise. Additionally, it may be advantageous for controlling blood sugar, arterial stiffness, sympathetic drive, and the structure of the heart—particularly the left atrium, which is prone to atrophy. Research has indicated that regular engagement in physical activity can lower the frequency of atrial fibrillation (AF) episodes [56]. It's crucial to remember, though, that research points to a possible increased risk of AF in relation to vigorous physical exercise. Generally speaking, maintaining an ideal level of physical activity can help lower the risk of atrial fibrillation (AF) and the difficulties that come with it [57].

Moderate-Intensity Exercise:

For individuals with atrial fibrillation (AF), a suggested weekly exercise threshold is 360–720 MET-minutes, or 60–120 minutes of moderate–to–intense exercise. This is how a cardiac rehabilitation program usually works. It is possible to reduce the number of non-responders and raise the possibility of successful outcomes by gradually increasing the dose to 1000–1499 MET-minutes/week. This can be accomplished by implementing a tailored and progressive rehabilitation program. [57,58].

Non-Traditional Exercise Approaches:

Yoga and Quality of Life: Non-traditional exercises, such as Yoga, may offer promising benefits for patients with AF. Yoga combines physical postures, breathing exercises, and meditation, potentially contributing to improved quality of life and physical capacity [59]. The holistic approach of Yoga may address both physical and psychological aspects of well-being.

Short-Term Exercise-Induced Cardioprotection:

Given that short-term exercise-induced cardioprotection has been demonstrated to have protective effects on the cardiovascular system, it is especially pertinent when considering cardiac rehabilitation for atrial fibrillation (AF) patients. Research has indicated that brief bursts of exercise can mitigate the damage done to the heart and blood vessels as a result of reperfusion and ischemia,

hence offering prompt cardioprotection [60]. Furthermore, it has been discovered that individuals who have had surgical aortic valve replacement (SAVR) benefit from short-term exercise training in terms of arterial blood pressure and QT dispersion [61]. Short-term exercise may have a role in neuroprotection following a stroke, as acute exercise has also been demonstrated to enhance stroke outcomes by inducing activation of endothelial nitric oxide synthase [62]. This is particularly relevant in the context of AF rehabilitation, where integrating short-term exercise interventions may yield positive outcomes.

Non-Response to Exercise Training:

Individual Variability: The idea of 'non-response' to exercise training underscores the individual variability in how individuals may adapt to exercise. Some individuals may not experience the expected cardiovascular benefits, emphasizing the need for personalized exercise prescriptions in AF rehabilitation programs [63,64].

Risk of Excessive Endurance Exercise:

Excessive endurance exercise, such as long-distance running, may induce physiological stress that could contribute to arrhythmogenic changes in the atria. Several studies have found an increased risk of atrial fibrillation (AF) in endurance athletes, particularly in men [65,66]. The relationship between endurance training and AF is complex, with factors such as cardiac adaptations to exercise, disturbances in cardiac injury biomarkers, and sex differences playing a role [67]. Endurance athletes often exhibit cardiac remodeling, including left atrial dilation, which is associated with AF in the general population [68]. However, it is important to note that atrial dilation in athletes is part of a physiological response to exercise, and functional parameters may help differentiate between physiological and pathological atrial remodeling [69].

In summary, physical activity plays a crucial role in managing AF risk and progression. The recommendations for exercise intensity, the exploration of non-traditional exercises like Yoga, and considerations of short-term cardioprotection and individual variability underscore the need for a personalized and balanced approach to exercise in AF rehabilitation. Healthcare providers should tailor exercise prescriptions based on individual characteristics, emphasizing both the cardiovascular benefits and potential risks associated with different exercise modalities.

V. Comprehensive Risk Factor Modification:

A comprehensive approach to risk factor modification for atrial fibrillation (AF) involves addressing multiple factors simultaneously. This includes lifestyle interventions such as weight management, blood pressure control, and maintaining a healthy lipid profile [70,71]. Weight loss, specifically from a body mass index (BMI) above 30 kg/m2, and the favorable effect on blood concentrations of biomarkers related to atrial fibrillation (AF) involves intricate pathophysiological mechanisms [13]. Here's a discussion on the pathophysiology of this relationship.

Inflammation and Adipose Tissue:

Adipokines: Adipose tissue, especially visceral fat, is known to produce pro-inflammatory cytokines and adipokines. Elevated levels of these substances contribute to a chronic inflammatory state, which has been linked to the development and progression of AF. Eating can aggravate atrial fibrillation (AF) by inducing atrial remodeling through various pathways, including fatty infiltration, oxidative stress, inflammation, fibrosis, and autonomic nervous system stimulation. It is possible to evaluate EAT thickness and volume accurately using a variety of imaging techniques, which makes it a promising imaging marker for risk assessment and cardiovascular outcome prediction. Specific medicines for eating disorders have not yet received approval, however EAT has been suggested as a viable therapeutic target [72–74].

Inflammatory Biomarkers: Weight loss, particularly in the context of reducing excess adipose tissue, can lead to a decrease in the release of inflammatory biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). This reduction in systemic inflammation may have a positive impact on the atrial myocardium, potentially attenuating the proarrhythmic environment [75–77].

Cardiac Remodeling:

Fatty Infiltration: Fatty infiltration in the atrial myocardium is linked to obesity and results in structural and electrical changes. Losing weight can stop or reverse this process, which would help the structure and function of the atrial tissue return to normal [78].

Fibrosis Reduction: Excessive adiposity is linked to atrial fibrosis, a common finding in individuals with AF. Weight loss may mitigate fibrotic changes by reducing the mechanical stretch on the atrial tissue, thus influencing the structural substrate for AF [79].

Metabolic Factors:

Insulin Resistance: A pathological condition known as insulin resistance (IR) occurs when cells do not react to the insulin hormone as they should, which results in poor glucose disposal. It is associated with atrial fibrillation (AF), diabetes, obesity, inflammation, and cardiovascular disorders—all of which are risk factors for AF. Obesity is another pathophysiologic component of type 2 diabetes mellitus that is linked to IR. Once hyperglycemia is evident, insulin resistance can be used as a therapeutic target and is a strong predictor of the development of diabetes in the future. Diabetes, prediabetes, and the metabolic syndrome all share IR. People who have type 2 diabetes frequently experience undiagnosed earlier stages of prediabetes and insulin resistance. While metabolic syndrome and insulin resistance are risk factors for AF episodes, not all clinical observations have supported them [80]. There is a strong correlation between diabetes and the incidence of atrial fibrillation (AF); meta-analyses show that people with type 2 diabetes had an increased risk of AF by 30.0–40.0%, even after controlling for hyperthyroidism, hypertension, BMI, renal disease, smoking, and coronary heart disease [81,82]

Dyslipidemia:

Dyslipidemia, characterized by elevated LDL cholesterol, low HDL cholesterol, and/or elevated triglyceride levels, has been associated with AF [83]. Studies have demonstrated that weight loss interventions, such as exercise, laparoscopic sleeve gastrectomy, and surgical removal of ACTH-secreting pituitary adenomas, can result in changes in specific lipid species and overall lipid levels [84]. These changes in lipid metabolism have been associated with improvements in BMI, glycated hemoglobin, triglyceride, and total cholesterol levels [85]. Therefore, weight loss interventions may contribute to a less arrhythmogenic environment by improving lipid profiles and reducing the risk of dyslipidemia-related complications, including AF.

Hemodynamic Effects:

Reduced Cardiac Load: Excess weight places an increased load on the heart, potentially contributing to atrial stretch and dilation. Weight loss can alleviate this hemodynamic burden, reducing atrial pressure and decreasing the likelihood of atrial stretch-related triggers for AF [86,87]. Bariatric surgery-induced weight loss has been shown to improve left atrial mechanical function, as measured by longitudinal strain, which is an independent imaging biomarker of increased AF and HF risk [88]. In patients who achieved effective weight loss with bariatric surgery, alterations in P-wave related atrial arrhythmia predictors, such as P wave dispersion and P wave peak time, were observed, indicating positive effects on the regression of ECG parameters that are predictors of atrial arrhythmias, particularly AF [89].

Systemic Effects:

Sleep Apnea and Hypertension:

A meta-analysis of 54,271 patients found that the incidence of AF is 88% higher in patients with OSA. Age and hypertension independently strengthen this association, suggesting that OSA treatment could help reduce AF recurrence [90].Weight loss has been associated with improvements in conditions often linked to obstructive sleep apnea (OSA) and hypertension. OSA is strongly associated with obesity, and intentional weight reduction in people with obesity and OSA has been shown to result in improvements in OSA severity [91]. Additionally, OSA and hypertension often coexist, and treating OSA can help improve hypertension [92]. However, while weight loss has been shown to improve various cardiovascular risk factors associated with OSA, such as HbA1c, systolic blood pressure, HDL cholesterol, and triglycerides, the effects on cardiovascular events have not been demonstrated [93]. Nevertheless, a small weight loss in a short period of time has been shown to have beneficial effects on central hemodynamic parameters, arterial stiffness, and autonomic activity in

obese individuals with non-severe sleep apnea [94]. Therefore, weight loss may indirectly contribute to a reduction in AF risk by improving conditions such as OSA and hypertension, but further research is needed to establish the direct impact on AF risk.

Anti-inflammatory Effects of Exercise:

Physical Activity:

There are several physiological reasons why exercise has been demonstrated to have anti-inflammatory effects. First of all, people with chronic inflammation frequently have high levels of pro-inflammatory cytokines like TNF-α and IL-6, which can be decreased by regular physical activity. Second, pro-inflammatory cytokines can be countered by exercise by increasing the production of anti-inflammatory cytokines like IL-10. Exercise can also increase the synthesis of heat shock proteins, which shield cells from oxidative damage and inflammation [95–97]. In conclusion, regular exercise can have significant anti-inflammatory effects, which can contribute to the reduction of systemic inflammation. This can further mitigate the risk of atrial fibrillation, a common heart rhythm disorder. Therefore, incorporating regular physical activity into one's lifestyle can be a beneficial strategy for maintaining cardiovascular health.

Lifestyle risk factors such as hypertension, sleep apnea, obesity (BMI>30 kg/m2), alcohol, and smoking have been identified as independent predictors of AF [98]. Comprehensively managing these risk factors has been shown to improve outcomes in AF patients. Therefore, a holistic approach that includes weight management and addressing other lifestyle risk factors is crucial in reducing the development and progression of AF.

VI. Lifestyle Modification in Primary Prevention

Lifestyle modifications play a crucial role in mitigating the risk of atrial fibrillation (AF) before its onset [99]. However, implementing these changes on a broader scale poses challenges. One challenge is the incomplete correction of modifiable risk factors, such as obesity, hypertension, and hyperlipidemia [100]. Another challenge is the lack of evidence from randomized controlled trials on the effects of integrated AF lifestyle programs [101]. Overcoming these barriers requires personalized risk factor treatment programs, patient education, and durable lifestyle management [102]. Additionally, the use of technology-supported interventions, such as e-health platforms, can enhance the effectiveness of lifestyle therapies.

The HARMS2-AF score is a lifestyle risk score that helps identify individuals at risk of atrial fibrillation (AF) in the general population [103]. It was developed and validated using data from the UK Biobank and Framingham Heart Study cohorts. The score includes factors such as hypertension, age, body mass index, male sex, sleep apnea, smoking, and alcohol consumption as predictive variables for AF development. Physical inactivity and diabetes were not found to be significant predictors [104]. The HARMS2-AF score demonstrated good predictive performance and outperformed other risk models such as Framingham-AF and ARIC [105].

The FIND-AF algorithm can identify individuals at higher risk of incident atrial fibrillation (AF) with good performance. It also has the ability to predict the risk of other conditions and death [106]. In a study using UK primary care electronic health records, FIND-AF demonstrated robust performance in identifying individuals at higher risk of AF within the next 6 months[106]. These individuals had a significantly higher risk of developing a range of other conditions including heart failure, stroke, peripheral vascular disease, and diabetes, among others. Additionally, they had a higher risk of death, accounting for a majority of cardiovascular deaths [107].

This lifestyle risk score may be useful in identifying individuals who are at risk of developing AF and can assist in population screening efforts.

VII. Critical Analysis of Clinical Trials and Studies

The collective analysis of the studies underscores the pivotal role of lifestyle modifications in managing atrial fibrillation (AF). Randomized clinical trials, such as Abed HS et al. (108) and the REVERSE-AF study by Middeldorp ME et al. (109), provide robust evidence supporting the efficacy of weight reduction and comprehensive risk factor management in reducing AF symptom burden. The significance of aggressive risk factor reduction is echoed in Pathak RK et al.'s (110) cohort study,

emphasizing the importance of a holistic approach in improving outcomes, particularly in the context of AF ablation.

Epidemiological studies and reviews by Mozaffarian D et al. (111) contribute essential population-level insights, with the former establishing prevalence statistics and the latter delving into the components of a cardioprotective diet. Large cohort studies, such as those conducted by Mora S et al. (112) and Huxley RR et al. (113), reinforce the association between physical activity, cardiovascular risk factors, and the onset of AF. Kwok CS et al.'s (114) meta-analysis further strengthens the link between AF and dementia, drawing attention to the multifaceted impact of AF beyond cardiovascular implications.

Wang TJ et al.'s (115) cohort study, with its substantial sample size of 22,005 participants, contributes significantly to our understanding of atrial fibrillation (AF) risk factors. The robustness of the large cohort enhances the reliability of the findings, and a P-value of <0.001 adds statistical strength to the identification of obesity as a risk factor.

In contrast, the pilot study conducted by Lampert R et al. (116) explores lifestyle modification's potential in alleviating AF symptoms. The study's strength lies in its initial investigation into the promise of lifestyle changes. However, the limitation of a small sample size restricts the generalizability of the findings. To validate the observed effects of lifestyle modification on AF symptoms, larger and controlled studies are essential. While pilot studies are pivotal for generating hypotheses, further research with more extensive participant cohorts is necessary to establish the efficacy of lifestyle interventions in managing AF symptoms comprehensively.

Mozaffarian D et al.'s (117) review provides a comprehensive exploration of the components of a cardioprotective diet, contributing significantly to a holistic understanding of cardiovascular health. The strengths of the study lie in its in-depth analysis, offering insights into dietary factors that may positively impact cardiovascular outcomes. However, akin to Lavie CJ et al. (118), the study is susceptible to potential biases associated with the review process. Review articles, by nature, rely on the selection and interpretation of existing studies, introducing the possibility of bias in the inclusion of studies and the synthesis of evidence. Despite this limitation, Mozaffarian D et al.'s work remains valuable for its role in elucidating dietary components that may influence cardiovascular health, providing a foundation for future research and dietary recommendations.

Despite the promising findings, certain limitations are evident, such as the varied sample sizes and potential biases intrinsic to observational studies and reviews. The diversity in study methodologies highlights the need for a meticulous approach in interpreting results and generalizing findings to broader populations. Overall, the synthesis of existing evidence advocates for a comprehensive strategy incorporating lifestyle interventions in AF management, yet the methodological nuances emphasize the imperative for further well-designed clinical trials to validate and refine these approaches.

Discussion Section: Unraveling the Complexities of Atrial Fibrillation Management

The multifaceted nature of atrial fibrillation (AF) demands a comprehensive exploration of its etiology and management. This review delves into the evolving landscape of AF, scrutinizing traditional approaches, and highlighting the emerging significance of lifestyle modifications. As the global incidence of AF rises, the need for a paradigm shift towards a more integrative and personalized approach becomes increasingly evident.

The traditional focus on pharmacological and procedural interventions is being reevaluated, giving way to a more integrative approach that includes lifestyle modifications. The recognition of interleukins and inflammatory mediators as potential markers for AF diagnosis and cardiovascular events underscores the dynamic exploration of AF pathogenesis. Computational models are paving the way for novel anti-AF targets, signaling a departure from conventional therapeutic strategies. This paradigm shift acknowledges the limitations of current approaches and strives for a deeper understanding of AF etiology.

The escalating incidence of AF presents a formidable global health challenge, with significant links to stroke, heart failure, and cardiovascular morbidity. Aging populations and the increasing prevalence of risk factors like obesity and sedentary lifestyles amplify the urgency of addressing AF on a broader scale. The anticipated doubling of AF cases over the next five decades magnifies the

clinical implications and places a substantial burden on healthcare systems. Early detection, characterization, and risk stratification become imperative for effective clinical management.

Lifestyle modifications emerge as pivotal influencers in AF management, challenging traditional dogmas and encouraging a nuanced understanding of AF pathogenesis. Weight management, physical activity, dietary choices, and risk factor reduction are recognized as modifiable determinants influencing AF development and progression. The review emphasizes the need for tailored and balanced lifestyle interventions, acknowledging the complementary role they play alongside pharmaceutical and procedural solutions. The intricate interplay of genetic, inflammatory, and lifestyle factors is highlighted as a key focus in contemporary AF research.

The objective of the review is to synthesize the impact of lifestyle changes on AF management. Recognizing lifestyle factors as integral to AF pathogenesis, the review explores the potential benefits of virtual education programs, adaptive foraging, and culturally tailored interventions. From weight management in type 2 diabetes to aging in place preferences, lifestyle changes offer a diverse range of positive impacts on AF management and community stability. The objective is to provide a comprehensive understanding of how lifestyle modifications can positively influence diverse aspects of AF care.

The traditional approaches to AF management have primarily revolved around pharmacological agents and procedural interventions. While acknowledging their historical significance, the review critically assesses the limitations of antiarrhythmic medications and catheter ablation. The potential risks of proarrhythmia, side effects, and variable efficacy necessitate a deeper understanding of AF etiology. The importance of individualized ablation strategies and the potential impact on heart failure with preserved ejection fraction (HFpEF) underscore the complexities in selecting appropriate interventions for a heterogeneous population.

A holistic understanding of AF etiology demands consideration of factors beyond electrophysiology. Genetic predisposition, inflammatory processes, and lifestyle factors intricately shape the trajectory of AF. Familial forms of AF, mutations in potassium and sodium channel genes, and the intricate web of inflammatory pathways reveal the multifaceted nature of AF pathogenesis. The complex interplay between inflammation and AF creates a feedback loop, emphasizing the need for interventions that break this cycle.

Lifestyle factors, including dietary habits, physical activity levels, cardiovascular health, and BMI, are recognized as modifiable determinants influencing AF development and progression. The review emphasizes the importance of considering lifestyle factors in the prevention and management of AF. Dietary influences, the complex relationship between specific dietary patterns and AF, and the impact of physical activity underscore the need for a nuanced and individualized approach to lifestyle modifications.

A comprehensive approach to risk factor modification involves addressing multiple factors simultaneously. Inflammation and adipose tissue dysfunction, metabolic factors like insulin resistance and dyslipidemia, hemodynamic effects, and systemic considerations are interconnected contributors to AF development. Weight loss is identified as a central element in reducing systemic inflammation, fibrotic changes, and the hemodynamic burden on the heart. The review discusses the intricate pathophysiological mechanisms through which weight loss positively influences biomarkers related to AF pathways.

While acknowledging challenges in implementing lifestyle modifications on a broader scale, the review discusses potential solutions. Technology-supported interventions, lifestyle risk scores like HARMS2-AF and FIND-AF, and the importance of personalized risk factor treatment programs offer promising avenues. Despite incomplete correction of modifiable risk factors and the lack of robust evidence from randomized controlled trials.

Limitations:

1. **Heterogeneity in Study Designs:** The included studies in this review exhibit heterogeneity in terms of study designs, populations, and methodologies. Variability in the duration and intensity of lifestyle interventions, as well as differences in patient demographics, may contribute to challenges in directly comparing and generalizing findings.

2. **Publication Bias:** The possibility of publication bias exists, as studies reporting positive outcomes may be more likely to be published. This bias could lead to an overestimation of the positive effects of lifestyle modifications on atrial fibrillation (AF) management.

3. **Short-Term Follow-up Periods:** Some studies may have relatively short follow-up periods, limiting the ability to assess the long-term sustainability and efficacy of lifestyle interventions in preventing or managing AF. Longitudinal studies with extended follow-up durations are crucial to understanding the durability of lifestyle effects.

4. **Limited Randomized Controlled Trials (RCTs):** The review may be constrained by the availability of RCTs specifically designed to investigate lifestyle modifications in AF. RCTs are considered the gold standard, but their scarcity in this context may hinder robust conclusions.

5. **Diversity in AF Populations:** The generalization of findings to diverse populations may be challenging, given variations in genetic predispositions, lifestyle patterns, and comorbidities across different regions and ethnicities. Future research should aim for a more comprehensive representation of global AF populations.

6. **Self-Reported Lifestyle Data:** Some studies may rely on self-reported data for lifestyle factors, introducing the potential for recall bias and inaccuracies. Objective measures and standardized assessments could enhance the reliability of lifestyle information.

7. **Lack of Consistency in Biomarker Assessment:** Variability in the assessment and interpretation of biomarkers associated with AF, such as inflammatory markers or adipokines, may impede the synthesis of conclusive evidence. Standardization in biomarker evaluation protocols is essential for consistency.

Suggestions for Future Research:

1. **Longitudinal RCTs with Diverse Populations:** Future research should prioritize well-designed, longitudinal RCTs that encompass diverse populations to enhance the generalizability of findings. These trials should consider variations in genetic backgrounds, socio-economic factors, and lifestyle patterns.

2. **Standardized Outcome Measures:** Establishing standardized outcome measures for lifestyle interventions in AF research is crucial. Consistent assessment protocols for biomarkers, arrhythmia recurrence, and patient-reported outcomes will facilitate more reliable comparisons across studies.

3. **Incorporate Advanced Technologies:** Integrating advanced technologies, such as wearable devices and mobile health applications, can provide real-time data on lifestyle factors and AF outcomes. This approach enhances data accuracy and allows for continuous monitoring, offering a more comprehensive understanding of the intervention's impact.

4. **Collaborative Multicenter Studies:** Large-scale, collaborative multicenter studies can address the limitations associated with individual studies. Pooling resources and data from multiple centers increase statistical power, allowing for a more robust analysis of lifestyle interventions' effectiveness.

5. **Focus on Mechanistic Insights:** Future research should delve deeper into the mechanistic aspects underlying the impact of lifestyle modifications on AF. Investigating the molecular and cellular pathways involved will contribute to a more nuanced understanding of how lifestyle influences the pathophysiology of AF.

6. **Inclusion of Patient-Centered Outcomes:** Emphasizing patient-centered outcomes, such as quality of life, symptom burden, and psychological well-being, in addition to traditional clinical endpoints, can provide a more comprehensive evaluation of the holistic benefits of lifestyle modifications for individuals with AF.

7. **Evaluate Cost-Effectiveness:** Assessing the cost-effectiveness of lifestyle interventions compared to traditional pharmacological or procedural approaches is essential for informing healthcare policies. Understanding the economic implications will contribute to the integration of lifestyle modifications into routine AF management strategies.

References

1. Mohammad, Erfan, Lotfi., P., S., Pezeshki., Nima, Rezaei. (2023). The role of interleukins in pathogenesis and prognosis of atrial fibrillation. Expert Review of Clinical Immunology. https://doi.org/10.1080/1744666X.2023.2196013

2. Ozan, Demirel., Alexander, E., Berezin., Moritz, Mirna., Elke, Boxhammer., S, X, Gharibeh., Uta, C., Hoppe., Michael, Lichtenauer. (2023). Biomarkers of Atrial Fibrillation Recurrence in Patients with Paroxysmal or Persistent Atrial Fibrillation Following External Direct Current Electrical Cardioversion. Advances in Cardiovascular Diseases. https://doi.org/10.3390/biomedicines11051452

3. Haibo, Ni., Stefano, Moretti., Xianwei, Zhang., Dobromir, Dobrev., Eleonora, Grandi. (2022). Integrative human atrial modeling unravels interactive PKA and CaMKII signaling as key determinant of atrial arrhythmogenesis. bioRxiv. https://doi.org/10.1101/2022.04.27.489795

4. Padmini, Sirish., Jun, Yang., Esha, Datta., Uma, N, Srivatsa., Bob, Kiaii., Leighton, T., Izu., Bruce, D., Hammock., Nipavan, Chiamvimonvat. (2022). Abstract 14554: Novel Upstream Targets for Atrial Fibrillation. Circulation. https://doi.org/10.1161/circ.146.suppl_1.14554

5. Arnela, Saljic., Jordi, Heijman., Dobromir, Dobrev. (2022). Emerging Antiarrhythmic Drugs for Atrial Fibrillation. International Journal of Molecular Sciences. https://doi.org/10.3390/ijms23084096

6. Angela, Marie, Hall., Andrew, R.J., Mitchell., Lisa, Ashmore., Carol, Holland. (2022). Atrial fibrillation prevalence and predictors in patients with diabetes: a cross-sectional screening study.. the british journal of cardiology. https://doi.org/10.5837/bjc.2022.008

7. Anthony, H., Kashou., Peter, A., Noseworthy. (2021). Predicting incident atrial fibrillation in sinus rhythm: more than just trusting the 'black box'.. Heart. https://doi.org/10.1136/HEARTJNL-2021-319385

8. Agnieszka, Kotalczyk., Agnieszka, Kotalczyk., Gregory, Y.H., Lip., Gregory, Y.H., Lip., Gregory, Y.H., Lip. (2021). Disparities in atrial fibrillation: a call for holistic care. https://doi.org/10.1016/J.LANEPE.2021.100160

9. Roberta, Rossini., Andrea, Peirone. (2022). When to set anticoagulant therapy in asymptomatic AF? looking for a cut-off duration. European Heart Journal Supplements. https://doi.org/10.1093/eurheartjsupp/suac086

10. B., Foster., Adnan, Liaqat., Awais, Farooq., SG, Kulkarni., Saikiran, Mandyam., Pooja, Patak., Morteza, Mahdoodi, Zaman., Paramjit, Kaur., Sebastian, Tosto., Arthur, C., Kendig. (2022). Temporal Trends for Patients Hospitalized With Atrial Fibrillation in the United States: An Analysis From the National Inpatient Sample (NIS) Database 2011-2018. Cureus. https://doi.org/10.7759/cureus.25694

11. Paul, Mihas., Lindsey, Rosman., Tiffany, Armbruster., Jennifer, Walker., Zachariah, Deyo., Anil, K., Gehi. (2023). Assessing a Virtual Education Intervention for Patients With Atrial Fibrillation: A Qualitative Study of Patient Perceptions.. Kardiyovasküler hemşirelik dergisi. https://doi.org/10.1097/JCN.0000000000000984

12. Thomas, P., West. (2023). Assessing a Virtual Education Intervention for Patients With Atrial Fibrillation. Journal of Cardiovascular Nursing. https://doi.org/10.1097/jcn.0000000000000984

13. L., Li., A., Alonso., Dora, Romaguera., Ángel, M., Alonso-Gómez., Cristina, Razquin., Lucas, Tojal-Sierra., Miquel, Fiol., Miguel, Ángel, Martínez-González., Vinita, Subramanya., Jorge, Salas-Salvadó., M, Fito., Estefanía, Toledo. (2023). Effect of an intensive lifestyle intervention on circulating biomarkers of atrial fibrillation-related pathways among adults with metabolic syndrome. medRxiv. https://doi.org/10.1101/2023.04.28.23288131

14. Ana, Lorenzo-Almorós., J., Casado, Cerrada., Luis, Antonio, Alvarez-Sala, Walther., Manuel, Méndez, Bailón. (2023). Atrial Fibrillation and Diabetes Mellitus: Dangerous Liaisons or Innocent Bystanders?. Stomatology. https://doi.org/10.3390/jcm12082868

15. Léo, Ledru., Jimmy, Garnier., Océane, Guillot., Camille, Noûs., Sébastien, Ibanez. (2023). Is adaptive foraging adaptive? A resource-consumer eco-evolutionary model. bioRxiv. https://doi.org/10.1101/2023.03.22.533765

16. Emmanuel, Ekpor., Samuel, Akyirem., Precious, Adade, Duodu. (2023). Prevalence and associated factors of overweight and obesity among persons with type 2 diabetes in Africa: a systematic review and meta-analysis. Annals of Medicine. https://doi.org/10.1080/07853890.2023.2182909

17. Zhong, He., Cailing, Jiang. (2023). Aging in Place or Institutionalization? A Multiscale Analysis of Independent-Living Older Adults From Four Large Cities in China's Yangtze River Delta. Innovation in Aging. https://doi.org/10.1093/geroni/igad014

18. Tim, Sweijs. (2023). Antiarrhythmic drugs for atrial fibrillation in the outpatient setting. Minerva Medica. https://doi.org/10.23736/s0026-4806.23.08524-5

19. Alvaro, Lladser. (2022). Pharmacological Management of Atrial Fibrillation: A Century of Expert Opinions in Cecil Textbook of Medicine. American Journal of Therapeutics. https://doi.org/10.1097/mjt.0000000000001464

20. (2022). Medical, Interventional, and Surgical Treatment Strategies for Atrial Fibrillation.. Deutsches Arzteblatt International. https://doi.org/10.3238/arztebl.m2021.0303

21. Luigi, Sciarra., Antonio, Scarà. (2023). Will the blooming of artificial intelligence modify our approach to atrial fibrillation cure?. Journal of Cardiovascular Electrophysiology. https://doi.org/10.1111/jce.15907

22. Nicolas, Johner. (2022). Safety, Efficacy and Prognostic Benefit of Atrial Fibrillation Ablation in Heart Failure with Preserved Ejection Fraction. Arrhythmia & electrophysiology review. https://doi.org/10.15420/aer.2022.10

23. Bharat, K., Kantharia. (2022). Left Atrial Appendage Occlusion Versus Anticoagulation in Atrial Fibrillation: Equipoise When Bleeding Risk Is High. Venereal Disease Information. https://doi.org/10.7326/M22-2271

24. Jarosław, Karwowski., Jerzy, Rekosz., Mateusz, Solecki., Renata, Maczyńska-Mazuruk., Karol, Wrzosek., Joanna, Sumińska-Syska., Mirosław, Dłużniewski. (2022). Electric cardioversion in patients treated with oral anticoagulants: embolic material in the left atrial appendage.. Cardiovascular journal of South Africa : official journal for Southern Africa Cardiac Society [and] South African Society of Cardiac Practitioners.

25. Kamel H, Elkind MSV. Genetics and the Quest to Define Sources of Cardiac Embolism. Stroke. 2023 Jul;54(7):1786-1788. https://doi.org/10.1161/STROKEAHA.123.043488. Epub 2023 Jun 26. PMID: 37363943; PMCID: PMC10313158.

26. Okamura T, Quan NS, Kobayashi T. Development of an AI System to Monitor Atrial Fibrillation with an ECG-based Stroke Potential Detection Engine Running in the Cloud. Research Square; 2023. https://doi.org/10.21203/rs.3.rs-2769048/v1.

27. Ning, Huang. (2022). Determinants and therapeutic potential of calcium handling abnormalities in atrial fibrillation: what can we learn from computer models?. The Journal of Physiology. https://doi.org/10.1113/jp283817

28. Medhat, Ashmawy., Ehab, Abdellatif, El-Gendy., Amany, Allaithy., Ahmed, E., I., Abu, Zarad. (2022). Clinical and Echocardiographic Predictor of Atrial Fibrillation in Patient with Rheumatic Mitral Valve Disease. Cardiology and angiology: an international journal. https://doi.org/10.9734/ca/2022/v11i430221

29. Peter, A., Noseworthy. (2022). Artificial intelligence and atrial fibrillation. Journal of Cardiovascular Electrophysiology. https://doi.org/10.1111/jce.15440

30. Xiaoqian, Zhou., Lan, Ren., Jian, Huang., Yinhui, Zhang., Ying, Cai., Jielin, Pu. (2023). Novel SCN5A frame-shift mutation underlying in patient with idiopathic ventricular fibrillation manifested with J wave in inferior lead and prolonged S-wave in precordial lead. Experimental and Therapeutic Medicine. https://doi.org/10.3892/etm.2023.11986

31. C, Paludan-Muller., Oliver, Bundgaard, Vad., Klaus, Kahnert., Gustav, Ahlberg., L., M., Monfort., S., A., Rand., L., C., Trudsoe., Laura, Andreasen., A., H., Christensen., Henning, Bundgaard., Alicia, Lundby., J.H.S, Hastrup, Svendsen., Morten, S., Olesen. (2022). Loss-of-function variants in founder population highlight atrial myopathy as susceptibility to atrial fibrillation. European heart journal. https://doi.org/10.1093/eurheartj/ehac544.2875

32. V, Jimenez-Sabado., Carmen, Tarifa., S, Casabella-Ramon., J, Montiel., Enrique, Rodríguez-Font., Morten, S., Olesen., Leif, Hove-Madsen. (2022). The rs13376333 risk allele mimics the effect of atrial fibrillation on SK-current density and afterdepolarizations in human atrial myocytes. European heart journal. https://doi.org/10.1093/eurheartj/ehac544.2978

33. Sefa, Ömür., Çağrı, Zorlu., Mustafa, Yilmaz. (2023). Comparison of the Relationship Between Inflammatory Markers and Atrial Fibrillation Burden.. https://doi.org/10.14744/AnatolJCardiol.2023.2927

34. Rafaqat S, Afzal S, Khurshid H, Safdar S, Rafaqat S, Rafaqat S. The Role of Major Inflammatory Biomarkers in the Pathogenesis of Atrial Fibrillation. J Innov Card Rhythm Manag. 2022 Dec 15;13(12):5265-5277. https://doi.org/10.19102/icrm.2022.13125

35. Yao Y, Yang M, Liu D, Zhao Q. Immune remodeling and atrial fibrillation. Front Physiol. 2022 Jul 22;13:927221. https://doi.org/10.3389/fphys.2022.927221. PMID: 35936905; PMCID: PMC9355726.

36. Yoshiko, Murakata., Fumi, Yamagami., Nobuyuki, Murakoshi., Dongzhu, Xu., Z, Song., Siqi, Li., Yuta, Okabe., Kazuhiro, Aonuma., Zixun, Yuan., Haruka, Mori., Kazutaka, Aonuma., Kazuko, Tajiri., Masaki, Ieda. (2023). Electrical, structural, and autonomic atrial remodeling underlies atrial fibrillation in inflammatory atrial cardiomyopathy. Frontiers in Cardiovascular Medicine. https://doi.org/10.3389/fcvm.2022.1075358

37. Christin, S., Börschel., Alfredo, Ortega-Alonso., Aki, S., Havulinna., Pekka, Jousilahti., Marko, Salmi., Sirpa, Jalkanen., Salomaa, Veikko., Teemu, J., Niiranen., Renate, B., Schnabel. (2023). Inflammatory proteomics profiling for prediction of incident atrial fibrillation. Heart. https://doi.org/10.1136/heartjnl-2022-321959

38. Emelia, J., Benjamin., Kevin, L., Thomas., Alan, S., Go., Patrice, Desvigne-Nickens., Christine, M., Albert., Alvaro, Alonso., Alanna, M., Chamberlain., Utibe, R., Essien., Inmaculada, Hernandez., Mellanie, True, Hills., Kiarri, N., Kershaw., Phillip, D., Levy., Jared, W., Magnani., Daniel, D., Matlock., Emily, C., O'Brien., Carlos, J., Rodriguez., Andrea, M., Russo., Elsayed, Z., Soliman., Lawton, S., Cooper., Sana, M., Al-Khatib. (2022). Transforming Atrial Fibrillation Research to Integrate Social Determinants of Health: A National Heart, Lung, and Blood Institute Workshop Report.. JAMA Cardiology. https://doi.org/10.1001/jamacardio.2022.4091

39. Anthony, Scarlett & Harrell, Rebecca & Khan, Saleen & Ha, Yumi & Qavi, Ahmed Hassaan & Pursell, Irion & Naniwadekar, Aditi & Travia, Kevin & Whited, Matthew & Sears, Samuel. (2022). AP-519-04 DEVELOPMENT OF THE ATRIAL FIBRILLATION "BEHAVIORAL CHA2DS2-VASC" IN ELECTROPHYSIOLOGY CLINICS. Heart Rhythm. 19. S90-S91. 10.1016/j.hrthm.2022.03.758.

40. Linzi, Li., Estefanía, Toledo., Dora, Romaguera., Ángel, M., Alonso-Gómez., Cristina, Razquin., Lucas, Tojal-Sierra., Miquel, Fiol., Miguel, Ángel, Martínez-González., Jordi, Salas-Salvadó., Montserrat, Fitó., Alvaro, Alonso. (2023). Abstract P101: Effect of an Intensive Lifestyle Intervention on Biomarkers of Atrial Fibrillation-Related Pathways Among Overweight Adults: The PREDIMED-PLUS Trial. Circulation. https://doi.org/10.1161/circ.147.suppl_1.p101

41. S., Tu., Celine, Gallagher., Adrian, D., Elliott., Kathryn, E., Bradbury., Gregory, M., Marcus., Dominik, Linz., Bradley, M., Pitman., Melissa, E., Middeldorp., Jeroen, M.L., Hendriks., Dennis, H., Lau., Prashanthan, Sanders., Christopher, X., Wong. (2023). Associations of dietary patterns, ultra-processed food and nutrient intake with incident atrial fibrillation. https://doi.org/10.1136/heartjnl-2023-322412

42. Hariharan, Raju., Chrishan, J., Nalliah. (2023). Association of diet with atrial fibrillation: villain or sidekick. https://doi.org/10.1136/heartjnl-2023-322897

43. Sicen, Wang., Ye, Cheng., Qi, Zheng., Xin, Su., Yingjian, Deng. (2023). Evaluating the association between dietary salt intake and the risk of atrial fibrillation using Mendelian randomization. Frontiers in Nutrition. https://doi.org/10.3389/fnut.2023.1073626

44. Ram, B., Singh., Fatemeh, Nabavizadeh., Jan, Fedacko., Dominik, Pella., Natalia, Vanova., Patrik, Jakabčin., Ghizal, Fatima., Rie, Horuichi., Toru, Takahashi., Viliam, Mojto., Lekh, Raj, Juneja., Shaw, Watanabe., Andrea, Jakabcinova. (2022). Dietary Approaches to Stop Hypertension via Indo-Mediterranean Foods, May Be Superior to DASH Diet Intervention. Nutrients, 15(1):46-46. https://doi.org/10.3390/nu15010046

45. Annie, Seixas, Bello, Moreira., Débora, Pinto, Gapanowicz. (2023). Diet Quality and Cardiovascular Health. International Journal of Cardiovascular Sciences. https://doi.org/10.36660/ijcs.20220215

46. S., Mambrini., Simone, Ravella., Marta, Pellizzari., Ramona, De, Amicis., Andrea, Foppiani., Alberto, Battezzati., Simona, Bertoli., Alessandro, Leone. (2023). Ultra-Processed Food Consumption and Incidence of Obesity and Cardiometabolic Risk Factors in Adults: A Systematic Review of Prospective Studies. Nutrients. https://doi.org/10.3390/nu15112583

47. Monica, Dinu., Daniela, Martini. (2023). Ultra-Processed Foods, Diet Quality and Human Health. Nutrients. https://doi.org/10.3390/nu15132890

48. Hao, Ma., Xuan, Wang., Xiang, Li., Yoriko, Heianza., Lu, Qi. (2023). 1379-P: Adding Salt to Foods and Risk of Severe Nonalcoholic Fatty Liver. Diabetes. https://doi.org/10.2337/db23-1379-p

49. Cong-jie, Wang., Guo-Shuai, Lin. (2023). Mendelian Randomization Analysis Reveals Causal Associations of Polyunsaturated Fatty Acids with Sepsis and Mortality Risk.. Infectious Diseases and Therapy. https://doi.org/10.1007/s40121-023-00831-z

50. Carolina, Bonilla., Guadalupe, Herrera., Mónica, Sans. (2023). What can Mendelian randomization contribute to biological anthropology?. American journal of biological anthropology. https://doi.org/10.1002/ajpa.24750

51. Bryon, J.T., Morgan., Jane, Richtsmeier., Oscar, Giménez., S., P., Brooks., Sophia, Green., John, Benedetti., Lawrence, H., Moulton., Harry, Wynn., Anatoly, Zhigljavsky. (2022). Mendelian randomization. Nature Reviews Methods Primers. https://doi.org/10.1038/s43586-021-00092-5

52. Kai, Wang., Xian, Shi., Ziwei, Zhu., Xingjie, Hao., Liangkai, Chen., S., Cheng., Roger, Foo., Chaolong, Wang. (2022). Mendelian randomization analysis of 37 clinical factors and coronary artery disease in East Asian and European populations. Genome Medicine. https://doi.org/10.1186/s13073-022-01067-1

53. Adrian, D., Elliott., C., Verdicchio., Rajiv, Mahajan., Melissa, E., Middeldorp., Celine, Gallagher., R., Mishima., Jeroen, M.L., Hendriks., Rajeev, K., Pathak., Gijo, Thomas., Dennis, H., Lau., Prashanthan, Sanders. (2022). An Exercise and Physical Activity Program in Patients With Atrial Fibrillation: The ACTIVE-AF Randomized Controlled Trial.. JACC: Clinical Electrophysiology. https://doi.org/10.1016/j.jacep.2022.12.002

54. James, A., Reiffel. (2023). The Party Should Not Last That Long. The Journal of innovations in cardiac rhythm management. https://doi.org/10.19102/icrm.2023.14013

55. Moo, Nyun, Jin., Pil, Sung, Yang., Changho, Song., Hee, Tae, Yu., Tae, Hoon, Kim., Jae, Sun, Uhm., Jung, Hoon, Sung., Hui, Nam, Pak., Moon, Hyoung, Lee., Boyoung, Joung. (2019). Physical Activity and Risk of Atrial Fibrillation: A Nationwide Cohort Study in General Population. Scientific Reports. https://doi.org/10.1038/S41598-019-49686-W

56. Sepehri Shamloo A, Arya A, Dagres N, Hindricks G. Exercise and Atrial Fibrillation: Some Good News and Some Bad News. Galen Med J. 2018 Nov 8;7:e1401. https://doi.org/10.22086/gmj.v0i0.1401. PMID: 34466451; PMCID: PMC8343702.

57. Buckley BJR, Risom SS, Boidin M, Lip GYH, Thijssen DHJ. Atrial Fibrillation Specific Exercise Rehabilitation: Are We There Yet? J Pers Med. 2022 Apr 10;12(4):610. https://doi.org/10.3390/jpm12040610. PMID: 35455726; PMCID: PMC9029299.

58. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice

Guidelines. Circulation. 2019 Sep 10;140(11):e596-e646. https://doi.org/10.1161/CIR.0000000000000678. Epub 2019 Mar 17. Erratum in: Circulation. 2019 Sep 10;140(11):e649-e650. Erratum in: Circulation. 2020 Jan 28;141(4):e60. Erratum in: Circulation. 2020 Apr 21;141(16):e774. PMID: 30879355; PMCID: PMC7734661.

59. Wahlstrom M, Rydell Karlsson M, Medin J, Frykman V. Effects of yoga in patients with paroxysmal atrial fibrillation - a randomized controlled study. Eur J Cardiovasc Nurs. 2017 Jan;16(1):57-63. https://doi.org/10.1177/1474515116637734. Epub 2016 Jul 7. PMID: 26976659.

60. D., Muktaly. (2022). Short-term exercise-induced protection of cardiovascular function and health: why and how fast does the heart benefit from exercise?. The Journal of Physiology. https://doi.org/10.1113/jp282000

61. V., Stoickov., Marina, Deljanin-Ilic., M., Stoickov., Ivan, Tomasic., I., Stoickov., S., Kostic., Dragan, Marinkovic., D., Simonovic. (2022). The influence of short-term exercise training on arterial blood pressure and qt dispersion in patience after surgical aortic valve replacement. Journal of Hypertension. https://doi.org/10.1097/01.hjh.0000838568.93520.2d

62. Sherif, Hafez., Mohammad, B, Khan., Mohamed, E., Awad., Jesse, D, Wagner., David, C., Hess. (2020). Short-Term Acute Exercise Preconditioning Reduces Neurovascular Injury After Stroke Through Induced eNOS Activation. Translational Stroke Research. https://doi.org/10.1007/S12975-019-00767-Y

63. Mary, O., Whipple., Dereck, L., Salisbury., Rebecca, J., Brown., Diane, Treat-Jacobson. (2022). Abstract 10271: Poor Response and Nonresponse to Clinically Available Supervised Exercise Therapy for Peripheral Artery Disease: A Pooled Analysis. Circulation. https://doi.org/10.1161/circ.146.suppl_1.10271

64. John, M., Moriarty. (2022). Issues on Trainability. Frontiers in Physiology. https://doi.org/10.3389/fphys.2021.790196

65. Nikola, Drca., Susanna, C., Larsson., David, Grannas., Mats, Jensen-Urstad. (2023). Elite female endurance athletes are at increased risk of atrial fibrillation compared to the general population: a matched cohort study. British Journal of Sports Medicine. https://doi.org/10.1136/bjsports-2022-106035

66. Camila, Cássia, Canzi. (2023). Atrial Fibrillation in Endurance Training Athletes: Scoping Review. Reviews in Cardiovascular Medicine. https://doi.org/10.31083/j.rcm2406155

67. Marco, Tatangelo., Marco, Rebecchi., Marianna, Sgueglia., Alessandra, Colella., Cinzia, Crescenzi., Germana, Panattoni., P., Ciampi., Oreste, Lanza., Emanuele, Canali., Leonardo, Calò. (2023). The Complex but Fascinating Relationship between Sport and Atrial Fibrillation: From Pathophysiology to the Clinical Scenario. Journal of Cardiovascular Development and Disease. https://doi.org/10.3390/jcdd10060255

68. Turid, Apelland., K., Janssens., Jan, Pål, Loennechen., Guido, Claessen., Eivind, Sørensen., Amy, Mitchell., Steve, Enger., Sophia, Onarheim., Jon, Magne, Letnes., Hielko, Miljoen., Arnljot, Tveit., Andre, La, Gerche., Marius, Myrstad. (2023). Effects of training adaption in endurance athletes with atrial fibrillation: protocol for a multicentre randomised controlled trial. BMJ open sport and exercise medicine. https://doi.org/10.1136/bmjsem-2023-001541

69. Sørensen E, Myrstad M, Solberg MG, Øie E, Platonov PG, Carlson J, Tveit A, Aarønaes M. Left atrial dyssynchrony in veteran endurance athletes with and without paroxysmal atrial fibrillation. Echocardiography. 2023 Jul;40(7):679-686. https://doi.org/10.1111/echo.15634. Epub 2023 Jun 6. PMID: 37279187.

70. Adrian, D., Elliott., C., Verdicchio., Rajiv, Mahajan., Melissa, E., Middeldorp., Celine, Gallagher., Dennis, H., Lau., Prashanthan, Sanders. (2022). Abstract 15833: Impact of Sex on Outcomes Following Aerobic Exercise Training in Patients With Symptomatic Atrial Fibrillation. Circulation. https://doi.org/10.1161/circ.146.suppl_1.15833

71. Wang, X., Zhang, Y., Ren, M., Guo, J., Li, Z., Wang, X., … & Hou, Y. (2023). Association of oxidative stress-related biomarkers and atrial fibrillation: a cross- sectional study.. https://doi.org/10.21203/rs.3.rs-3063179/v1

72. Soeren, Z., Diederichsen., K., Haugan., Axel, Brandes., C., Graff., Don, Krieger., Morten, S., Olesen., L, Koeber., Niels, Vejlstrup., Litten, Bertelsen., J.H.S, Hastrup, Svendsen. (2023). Epicardial adipose tissue and subclinical incident atrial fibrillation in a population at risk of stroke - a cardiac magnetic resonance imaging study. European journal of echocardiography. https://doi.org/10.1093/ehjci/jead119.081

73. Brooks, Willar., Khanh-Van, T., Tran., Timothy, P., Fitzgibbons. (2023). Epicardial adipocytes in the pathogenesis of atrial fibrillation: An update on basic and translational studies. Frontiers in Endocrinology. https://doi.org/10.3389/fendo.2023.1154824

74. Kiran, Upadhyay., William, H., Frishman. (2023). An Exploration of the Relationship Between Atrial Fibrillation and Obesity. Cardiology in Review. https://doi.org/10.1097/CRD.0000000000000490

75. Honghong, Wang. (2023). Data from Effects of a Caloric Restriction Weight Loss Diet and Exercise on Inflammatory Biomarkers in Overweight/Obese Postmenopausal Women: A Randomized Controlled Trial. https://doi.org/10.1158/0008-5472.c.6503982.v1

76. Duggan C, Tapsoba JD, Shivappa N, Harris HR, Hébert JR, Wang CY, McTiernan A. Changes in Dietary Inflammatory Index Patterns with Weight Loss in Women: A Randomized Controlled Trial. Cancer Prev

Res (Phila). 2021 Jan;14(1):85-94. https://doi.org/10.1158/1940-6207.CAPR-20-0181. Epub 2020 Aug 28. PMID: 32859616; PMCID: PMC7914258.

77. Hassan, Mahmoud, Hassanin., Usama, A., Khali., Amany, M, Sediq., Arafa, M., Elshabrawy. (2022). Effect of Weight Reduction on Inflammatory Mediators in Patients with and without Metabolic Syndrome. The Egyptian Journal of Hospital Medicine. https://doi.org/10.21608/ejhm.2022.256616

78. Limpitikul WB, Das S. Obesity-Related Atrial Fibrillation: Cardiac Manifestation of a Systemic Disease. J Cardiovasc Dev Dis. 2023 Jul 30;10(8):323. https://doi.org/10.3390/jcdd10080323. PMID: 37623336; PMCID: PMC10455513.

79. Yaacoub, Chahine., Bahareh, Askari-Atapour., Kirsten, T., Kwan., Carter, A., Anderson., Fima, Macheret., Tanzina, Afroze., Savannah, F, Bifulco., Matthew, D., Cham., Karen, G., Ordovas., Patrick, M., Boyle., Nazem, Akoum. (2022). Epicardial adipose tissue is associated with left atrial volume and fibrosis in patients with atrial fibrillation. Frontiers in Cardiovascular Medicine. https://doi.org/10.3389/fcvm.2022.1045730

80. Rafaqat, S., Rafaqat, S. & Rafaqat, S. Pathophysiological aspects of insulin resistance in Atrial Fibrillation: novel therapeutic approaches. Int J Arrhythm 23, 6 (2022). https://doi.org/10.1186/s42444-021-00057-5

81. Huxley RR, Filion KB, Konety S, Alonso A. Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. Am J Cardiol. 2011 Jul 1;108(1):56-62. https://doi.org/10.1016/j.amjcard.2011.03.004. Epub 2011 Apr 27. PMID: 21529739; PMCID: PMC3181495.

82. Aune D, Feng T, Schlesinger S, Janszky I, Norat T, Riboli E. Diabetes mellitus, blood glucose and the risk of atrial fibrillation: A systematic review and meta-analysis of cohort studies. J Diabetes Complications. 2018 May;32(5):501-511. https://doi.org/10.1016/j.jdiacomp.2018.02.004. Epub 2018 Feb 17. PMID: 29653902.

83. Tao, Lin., X., R., Liu. (2023). P-023 Weight loss in obese fathers improves hepatic lipid metabolism in offspring. Human Reproduction. https://doi.org/10.1093/humrep/dead093.390

84. Yoriko, Heianza., Qiaochu, Xue., Jennifer, Rood., C., Clish., George, A., Bray., Frank, M., Sacks., Lu, Qi. (2022). Abstract 048: Changes In Bile Acid Metabolism, Circulating MicroRNA-34a, And Improvements In Lipid Profiles In Response To Weight-loss Diets: The Pounds Lost Trial. Circulation. https://doi.org/10.1161/circ.145.suppl_1.048

85. K., Lin., Wei, Chen., Qiwei, Shen., Hui, Wang., Ruwen, Wang., Shanshan, Guo., Xianmin, Wu., Wei, Wu., Peijie, Chen., Yongfei, Wang., Hongying, Ye., Qiongyue, Zhang., Ru, Wang. (2023). Lipid Profiling Reveals Lipidomic Signatures of Weight Loss Interventions. Nutrients. https://doi.org/10.3390/nu15071784

86. Jakub, Strzelczyk., Piotr, Kalinowski., Krzysztof, Zieniewicz., Cezary, Szmigielski., Michal, Byra., Grzegorz, Styczynski. (2021). The Influence of Surgical Weight Reduction on Left Atrial Strain. Obesity Surgery. https://doi.org/10.1007/S11695-021-05710-5

87. Ersin, İbişoğlu., Bedrettin, Boyraz., Saime, Turgut, Güneş., Umeyir, Savur., Deniz, Dilan, Naki, Tekin., Aslan, Erdoğan., Yasar, Ozdenkaya., Emrah, Erdoğan., Ercan, Çeğilli., Fatih, Erkam, Olgun., Hacı, Murat, Güneş. (2021). Impact of surgical weight loss on novel P-wave-related variables which are nominated as predictors of atrial arrhythmias.. Pacing and Clinical Electrophysiology. https://doi.org/10.1111/PACE.14327

88. Sage, P., Kramer., David, K., Powell., Christopher, M., Haggerty., Cassi, M, Binkley., Andrea, C., Mattingly., Lisa, A., Cassis., Frederick, H., Epstein., Brandon, K., Fornwalt. (2013). Obesity reduces left ventricular strains, torsion, and synchrony in mouse models: a cine displacement encoding with stimulated echoes (DENSE) cardiovascular magnetic resonance study. Journal of Cardiovascular Magnetic Resonance. https://doi.org/10.1186/1532-429X-15-109

89. Shaimaa, Ahmed., Mostfa. (2018). Impact of obesity and surgical weight reduction on cardiac remodeling.. Indian heart journal. https://doi.org/10.1016/J.IHJ.2018.01.012

90. Amalia, Ioanna, Moula., Iris, Parrini., Cecilia, Tetta., Fabiana, Lucà., Gianmarco, Parise., Carmelo, Massimiliano, Rao., E, Mauro., Orlando, Parise., Francesco, Matteucci., Michele, Massimo, Gulizia., Mark, La, Meir., Sandro, Gelsomino. (2022). Obstructive Sleep Apnea and Atrial Fibrillation. Stomatology, 11(5):1242-1242. https://doi.org/10.3390/jcm11051242

91. Atul, Malhotra., Alexandra, M., Curtis., J., Dunn., Mathijs, C., Bunck., Josef, Bednarik. (2023). 0572 Weight reduction and the impact on apnea-hypopnea index: a meta-analysis. Sleep. https://doi.org/10.1093/sleep/zsad077.0572

92. Shyam, Chand, Chaudhary., Pankaj, Gupta., Kamal, Kumar, Sawlani., Kamlesh, K., Gupta., Ajay, K., Singh., Kauser, Usman., Vivek, Kumar., Dandu, Himanshu., Ajay, Verma., Abhishek, Singh. (2023). Obstructive Sleep Apnea in Hypertension. Cureus. https://doi.org/10.7759/cureus.38229

93. Ayyad, Alruwaily., Heshma, Alruwaili., John, F., Garvey., C., W., le, Roux. (2022). Can Weight Loss Improve the Cardiovascular Outcomes of Patients with Obesity and Obstructive Sleep Apnea?. Hearts. https://doi.org/10.3390/hearts3020008

94. Beom, Soo, Kim., Ji, Ho, Choi. (2023). Weight Loss for Obstructive Sleep Apnea: Pharmacological and Surgical Management. Journal of Rhinology. https://doi.org/10.18787/jr.2023.00010

95. Docherty, S., Harley, R., McAuley, J.J. et al. The effect of exercise on cytokines: implications for musculoskeletal health: a narrative review. BMC Sports Sci Med Rehabil 14, 5 (2022). https://doi.org/10.1186/s13102-022-00397-2

96. Scheffer DDL, Latini A. Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs. Biochim Biophys Acta Mol Basis Dis. 2020 Oct 1;1866(10):165823. https://doi.org/10.1016/j.bbadis.2020.165823.

97. Małkowska P, Sawczuk M. Cytokines as Biomarkers for Evaluating Physical Exercise in Trained and Non-Trained Individuals: A Narrative Review. Int J Mol Sci. 2023 Jul 6;24(13):11156. https://doi.org/10.3390/ijms241311156. PMID: 37446334; PMCID: PMC10342447.

98. Louise, Segan., R., E., Vega, Canovas., Shane, Nanayakkara., David, Chiang., Sandeep, Prabhu., Aleksandr, Voskoboinik., H., Sugumar., Li, Lin., Joseph, B, Morton., Andre, LaGerche., David, M., Kaye., Prashanthan, Sanders., Jonathan, M., Kalman., L., M., Kistler. (2023). New-onset atrial fibrillation prediction: the HARMS2-AF risk score.. European heart journal. https://doi.org/10.1093/eurheartj/ehad375

99. Ana, Lorenzo-Almorós., J., Casado, Cerrada., Luis, Antonio, Alvarez-Sala, Walther., Manuel, Méndez, Bailón. (2023). Atrial Fibrillation and Diabetes Mellitus: Dangerous Liaisons or Innocent Bystanders?. Stomatology. https://doi.org/10.3390/jcm12082868

100. Kara, Stout., M., Almerstani., Rees, Adomako., D., Shin., Ahmad, Aroudaky., Hannah, K, Tandon., J., William, Schleifer., Jason, Payne., Arthur, R., Easley., Faris, Khan., John, R., Windle., N., Goyal., Shane, F., Tsai., Daniel, G., Anderson., Thoetchai, Peeraphatdit., Niyada, Naksuk. (2023). Prevalence and Impact of Poorly Controlled Modifiable Risk Factors Among Patients Who Underwent Atrial Fibrillation Ablation.. American Journal of Cardiology. https://doi.org/10.1016/j.amjcard.2023.04.024

101. Aleksandr, I., Olesin., Irina, V., Konstantinova., Vladimir, Ivanov. (2022). Correction of Potentially Modifiable Components of Metabolic Syndrome for the Primary Prevention of Atrial Fibrillation in Comorbid Patients with Premature Atrial Complexes. Cardiac Arrhythmias. https://doi.org/10.17816/cardar105575

102. T.A.M., Vinck., Stacey, R, Slingerland., Marcel, van, 't, Veer., Marta, Regis., Jos-marien, Jansen., Edwin, R., van, den, Heuvel., Lukas, R.C., Dekker. (2023). Improving outcomes of AF ablation by integrated personalized lifestyle interventions: rationale and design of the prevention to improve outcomes of PVI (POP) trial. Clinical Research in Cardiology. https://doi.org/10.1007/s00392-023-02185-5

103. Segan L, Canovas R, Nanayakkara S, Chieng D, Prabhu S, Voskoboinik A, Sugumar H, Ling LH, Lee G, Morton J, LaGerche A, Kaye DM, Sanders P, Kalman JM, Kistler PM. New-onset atrial fibrillation prediction: the HARMS2-AF risk score. Eur Heart J. 2023 Sep 21;44(36):3443-3452. https://doi.org/10.1093/eurheartj/ehad375. PMID: 37350480.

104. Kara, Stout., Rees, Adomako., M., Almerstani., D., Shin., Hans, Tandon., Jessica, Schleifer., Jason, Payne., Arthur, R., Easley., Faris, Khan., John, R., Windle., Shane, F., Tsai., Daniel, G., Anderson., Niyada, Naksuk. (2022). Prevalence of modifiable risk factors and related poor cardiovascular outcomes following atrial fibrillation ablation. European heart journal. https://doi.org/10.1093/eurheartj/ehac544.432

105. Ramesh, Nadarajah., J.R., Wu., Darren, Hogg., K, R, Raveendra., Yoko, M., Nakao., Kojiro, Nakao., R., Arbel., Muriel, Haim., Doron, Zahger., Janet, Parry., Christopher, M., Bates., J., C., Cowan., Chris, P, Gale. (2023). Development, validation and outcomes associated with a risk prediction algorithm for incident atrial fibrillation: retrospective national cohort study of 2 081 139 individuals. Europace. https://doi.org/10.1093/europace/euad122.54

106. Jian-Hen, Wu., Ramesh, Nadarajah., Yoko, M., Nakao., Kazuhiro, Nakao., David, C., Hogg., Keerthenan, Raveendra., Ron, Arbel., Moti, Haim., Doron, Zahger., Campbell, Cowan., Chris, P, Gale. (2023). Incident cardiovascular, renal, metabolic diseases and death in individuals identified for risk-guided atrial fibrillation screening: a nationwide cohort study. Open heart. https://doi.org/10.1136/openhrt-2023-002357

107. Yung, Ta, Kao., Chun-Yao, Huang., Yu, Ann, Fang., Ju-Chi, Liu., T.H., Chang. (2023). Machine Learning-Based Prediction of Atrial Fibrillation Risk Using Electronic Medical Records in Older Aged Patients.. American Journal of Cardiology. https://doi.org/10.1016/j.amjcard.2023.03.035

108. Abed HS, Wittert GA, Leong DP, et al. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial. JAMA. 2013;310(19):2050-2060. https://doi.org/10.1001/jama.2013.280521.

109. Middeldorp ME, Pathak RK, Meredith M, et al. PREVEntion and regRessive Effect of weight-loss and risk factor modification on Atrial Fibrillation: the REVERSE-AF study. Europace. 2018;20(12):1929-1935. https://doi.org/10.1093/europace/euy174.

110. Pathak RK, Middeldorp ME, Lau DH, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. J Am Coll Cardiol. 2014;64(21):2222-2231. https://doi.org/10.1016/j.jacc.2014.09.028.

111. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation. 2015;131(4):e29-e322. https://doi.org/10.1161/CIR.0000000000000152.

112. Mora S, Cook N, Buring JE, Ridker PM, Lee IM. Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. Circulation. 2007;116(19):2110-2118. https://doi.org/10.1161/CIRCULATIONAHA.107.729939.

113. Huxley RR, Lopez FL, Folsom AR, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the Atherosclerosis Risk in Communities (ARIC) study. Circulation. 2011;123(14):1501-1508. https://doi.org/10.1161/CIRCULATIONAHA.110.009035.

114. Kwok CS, Loke YK, Hale R, Potter JF, Myint PK. Atrial fibrillation and incidence of dementia: a systematic review and meta-analysis. Neurology. 2011;76(10):914-922. https://doi.org/10.1212/WNL.0b013e31820f2e38

115. Wang TJ, Parise H, Levy D, et al. Obesity and the risk of new-onset atrial fibrillation. JAMA. 2004;292(20):2471-2477. https://doi.org/10.1001/jama.292.20.2471.

116. Lampert R, Burg MM, Batsford WP, McPherson CA, Jain D. Lifestyle modification for patients with atrial fibrillation: a pilot study. J Cardiovasc Nurs. 2012;27(2):137-146. https://doi.org/10.1097/JCN.0b013e31821c1d1a.

117. Mozaffarian D, Appel LJ, Van Horn L. Components of a cardioprotective diet: new insights. Circulation. 2011;123(24):2870-2891. https://doi.org/10.1161/CIRCULATIONAHA.110.968735.

118. Lavie CJ, Arena R, Swift DL, et al. Exercise and the cardiovascular system: clinical science and cardiovascular outcomes. Circ Res. 2015;117(2):207-219. https://doi.org/10.1161/CIRCRESAHA.117.305205.