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Lifestyle and atrial fibrillation

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Anna Vittoria Mattioli

Department of Biomedical Science,
University of Modena and RE, Via del
Pozzo 71, Modena 41100, Italy
Tel.: +39 59 422 4043
Fax: +39 59 205 5426
annavittoria.mattioli@unimore.it

Lifestyle factors, in particular dietary intake, have been recognized as important, modifiable risk factors for cardiovascular disease. Consuming a heart-healthy diet lowers the individual's risk for cardiovascular disease. Data on the relationship between lifestyle and atrial fibrillation are controversial; however, the strong association between obesity, atrial/ventricular dysfunction and a nonhealthy lifestyle and atrial fibrillation, suggests that a correction of nutritional habits could prevent the development of arrhythmias through a reduction of underlying cardiac diseases. Today, the Mediterranean diet is considered one of the most effective in terms of its prevention of cardiovascular disease.

KEYWORDS: alcohol • atrial fibrillation • caffeine • diet • lifestyle • obesity

Lifestyle factors, particularly dietary intake, have been recognized as important, modifiable risk factors for cardiovascular disease (CVD).

Consuming a heart-healthy diet (lower in saturated fats and rich in fruits and vegetables, whole grains, fish and lean meats; calorie controlled; and moderate sodium intake), as well as engaging in regular physical activity, lowers the individual's risk for CVD. The majority of studies evaluated the relationship between lifestyle and atherosclerosis and, subsequently, coronary artery disease, whereas little is known about the influence of lifestyle on arrhythmias.

The aim of this article is to review the evidence relating to some aspects of lifestyle and atrial fibrillation (AF) in order to provide both an understanding and limitations of our knowledge, as well as provide recommendations for patients with known or suspected arrhythmia with regards to lifestyle.

Atrial fibrillation is the most common arrhythmia in clinical practice. It is estimated to currently affect over 6 million patients in Europe and approximately 3 million in the USA, and this number is projected to at least double in the next 25 years owing to the aging population [1].

The mechanism by which lifestyle influences AF is related to the effects of nutritional and behavioral habits on the development of atherosclerotic plaque, so that the link with arrhythmias extends to coronary artery disease. Furthermore, lifestyle deeply influences the development of cardiac disease strictly related to AF, that is, hypertension, left ventricular hypertrophy and

cardiomyopathy. Historically, coronary artery disease and left ventricular cardiomyopathy have been regarded as the main causes of ventricular arrhythmia and sudden cardiac death (SCD). Similarly, in a substantial number of patients, AF develops in the presence of structural heart disease, however, in a number of patients it occurs in the absence of structural heart disease. It has been suggested that a nonhealthy lifestyle could also act as trigger for AF.

Diet, obesity & atrial fibrillation

The ongoing obesity epidemic, along with the health benefits of weight loss, has been well established and national dietary weight loss guidelines (i.e., energy-restricted, low in fat, high in carbohydrate) have been challenged [2]. Certain dietary patterns can influence cardiovascular health by modifying traditional risk factors such as obesity, dyslipidemia and hypertension, as well as new emerging risk factors; that is, systemic inflammation, insulin sensitivity, oxidative stress, endothelial dysfunction, prothrombotic status and cardiac arrhythmias [3,4]. Moreover, some dietary components, such as caffeine, alcohol and fish-derived long-chain polyunsaturated fatty acids (PUFAs), influence CVD morbidity and mortality [5–7].

However, the effect of dietary patterns and specific dietary factors on cardiac arrhythmias is not well established.

Obesity is a strong risk factor of CVD. Over the past decade, the prevalence of overweight individuals and obesity in the US

population including children and adolescents has increased [8]. Approximately 65% of US adults are classified as overweight and more than 30% of US adults are obese [9].

Currently, the typical American (Western) diet is estimated to derive 49% of its calories from carbohydrates, 34% from fat, and 12–16% from protein [10]. Proposals to alter the proportions and/or types of macronutrients in this diet have been made for weight loss and cardiovascular health [11]. The ideal strategy entails the intake of a low-calorie, low-fat diet; however, some alternative approaches including high protein and low carbohydrate have been proposed. Although restriction of caloric intake is an intuitive strategy to achieve weight loss, the effect of changes in dietary macronutrient composition has been a subject of greater controversy. Several randomized trials that compared low carbohydrate with low-fat diets in overweight/obese patients demonstrated that a low-carbohydrate diet appears more effective than a low-fat diet in causing short-term, albeit unsustainable, weight loss. One mechanism by which low-carbohydrate diets induce immediate weight loss is believed to be ketosis-induced diuresis and loss of appetite. Alternative mechanisms have included the highly restricted food choices that come with the simplistic design of the diet and the appetite-suppressing or satiety-inducing properties of the diet [12].

In the case of low-carbohydrate diets, there is a concern that excessive dietary protein intake and excessive fat intake can occur and potentially increase long-term risks for CVD. On the contrary, when dietary fat intake is severely restricted it could result in biochemical evidence of essential fatty acid deficiency. Some clinical consequences have been reported, including tachyarrhythmia, especially when low-fat intake persists for several years [13,14].

Obesity is an important risk factor of AF. The relationship between obesity and AF has been demonstrated in several population studies including the Framingham Heart study (FHS) and the Danish Diet, Cancer, and Health Study [15,16]. The Danish Study first reported an increased risk of AF by an increasing BMI. In that population the risk rises for about 8% per BMI unit increment [16]. The mechanism by which obesity contributes to an increased risk of AF is related to morphofunctional changes [17]. Obesity increases blood pressures, increases left ventricular volumes and hypertrophy, increases wall stress, and increases systolic and/or diastolic dysfunction [18]. In addition to left ventricular (LV) structural abnormalities, obesity also leads to left atrial (LA) enlargement, both from increased circulating blood volume, as well as abnormal LV diastolic filling. Weight reduction in obese subjects is associated with a regression of these abnormalities [19].

In the FHS, obese subjects showed a 45–50% increased risk for incident AF compared with subjects with normal BMI, independently from other cardiovascular risk factors [15]. In this cohort of patients, after adjustment for LA diameter, BMI was no longer associated with AF risk. The investigators concluded that the effect of obesity was mediated by LA dilatation. This hypothesis is strongly supported by data from Atrial Fibrillation Follow-up

Investigation of Rhythm Management (AFFIRM) study that found that obesity was associated with a higher incidence of AF recurrence and greater AF burden [20].

The primary therapeutic approach in obese patients is to decrease caloric intake and increase caloric expenditure by modifying lifestyle [16]. Physical activity is part of a healthy lifestyle. The health-promoting effects of regular physical activity on CVD are well established. Regular exercise directly and positively affects cardiac physiology (e.g., increased myocardial oxygen supply and enhanced myocardial contractility), both in the general population and in patients with CVD.

Different dietary components have been suggested as important modifiable risk factors for CVD. Although traditionally nutritional research has focused primarily on single nutrients or foods, interest is growing in dietary patterns that consider the complexity of the overall diet.

Some dietary patterns have shown positive effects on CVD. The Asian 'vegetable-rich' pattern, characterized by a frequent consumption of vegetables, fruit, soy products, seaweeds and fish is inversely related to cardiovascular mortality, whereas patterns characterized by a frequent consumption of meat and butter are directly related to CVD [21,22].

A very popular healthy diet is the Dietary Approaches to Stop Hypertension (DASH) diet, which is high in fruits and vegetables, moderate in low-fat dairy products and low in animal protein but with substantial amounts of plant protein from legumes and nuts. The DASH diet induces a reduction in both systolic and diastolic blood pressure among hypertensive and normotensive individuals [23]. In fact, this diet pattern shows greater improvement in blood pressure than one high in fruits and vegetables only. Weight is also directly associated with blood pressure. With rare exception, trials have documented that weight loss lowers blood pressure. No data are available on the effects of the DASH diet on cardiac arrhythmias, however, the reduction of blood pressure leads to a better performance of left ventricle and to a reduction of cardiac abnormalities strongly related to LA dilation and AF.

Today, the Mediterranean diet (Med Diet) is considered one of the best in terms of its prevention of CVD. A recent meta-analysis of over 1.5 million healthy subjects shows that a greater adherence to Med Diet is significantly associated with a reduced risk of overall mortality and cardiovascular mortality [24]. It has become customary to represent mediterranean dietary pattern in the form of a pyramid, the base of that refers to foods which are suggested to be consumed most frequently (i.e., nonrefined cereals and products such as whole grain bread, pasta, rice; vegetables, fruits, olive oil and non-fat or low-fat dairy products) and the top of the pyramid to those foods to be consumed rarely (red meat and meat products). The remaining foods occupy intermediate positions. Med Diet is a diet rich in fruits, vegetables, legumes, cereals and olive oil as the only source of fat, which are rich in vitamins C and E, β -carotene, selenium, α -tocopherol and flavonoids. Moreover, the Med Diet pattern is characterized by moderate consumption of wine, especially during meals, that has been shown to be beneficial, acting

positively on lipid metabolism, blood pressure, endothelial dysfunction and obesity. Compared with standard Western diets, the Med Diet is considered to be relatively high in α -linolenic acid (~2 g per day or 1% of total calories) and low in linoleic acid, with an ω -3: ω -6 ratio of 1:7 [24,25,26]. The Med Diet is more effective in promoting weight loss and lowering the ratio of total to high-density lipoprotein cholesterol in obese individuals than a low-fat diet [27].

The Med Diet is associated with a reduction in cardiac death, but the underlying mechanisms are poorly understood. It has been linked to beneficial effects on inflammatory status. Patients with AF have high levels of inflammatory markers, that is, C-reactive protein, IL-6 and TNF [28]. Inflammatory infiltration and fibrosis have been found in atrial biopsies of patients with lone atrial fibrillation suggesting a relationship between inflammation and AF, supporting the relationship between inflammatory status and arrhythmias [29]. However, it is not clear whether the inflammatory condition is the cause of AF, or the result of repeated attacks and a marker that arrhythmia is becoming established. Adherence to the Med Diet is associated with lower levels of C-reactive protein (HS-CRP) and IL-6 and other markers of endothelial function [30,31]. A study evaluating adherence to the Med Diet among healthy adults in the Attica region found that those in the highest tertile of adherence averaged 20% lower HS-CRP and 17% lower IL-6 levels, when compared with those in the lowest tertile [32].

The Med Diet is also associated with more favorable levels of adiponectin, an adipocytokine linked to cardiovascular risk [33]. Adiponectin is a protein secreted by adipose tissue involved in the development of atherosclerosis as demonstrated by its association with the stepwise progression of atherogenesis and, more importantly, the components of plaque vulnerability [34]. Although adiponectin is produced by adipocytes, plasma levels are actually inversely proportional to BMI and visceral adiposity. Vascular inflammation is characterized by increased adhesion molecule expression via proinflammatory cytokines such as IL-1, IL-8 and TNF- α . Adiponectin partakes in inflammatory factor propagation by adhesion molecule expression. In many studies assessing the health effects of the Med Diet, the authors have speculated about the biological processes that mediate its apparent effects, focusing on possible favorable effects of olive oil on blood lipids [35,36]. The olive oil, a good source of monounsaturated fatty acids (MUFAs), contains phenolic compounds that may have antioxidant, anti-inflammatory, and anti-thrombotic properties. The protective effect of the Med Diet has been attributed, at least in part, to the richness of this diet in antioxidants. Not all components of the Med Diet are protective, or at least they may not provide equal levels of protection. However, food items and nutrients could have a synergistic and antagonistic effect within a dietary pattern.

The complex relationship between diet and AF is also mediated by antioxidant intake. The total antioxidant capacity is strongly related to the consumption of fruit, vegetables and olive oil, and seems to be inversely associated with the consumption of red meat [32]. A greater adherence to the Med Diet is associated

with increased total antioxidant capacity as previously demonstrated by the ATTICA study. The protective effect is related to bioactive compounds in fruits and vegetables that reduce oxidative stress, a condition that arises when the formation of reactive oxidants and oxidative damage occurs [37]. Fruits and vegetables contain at least several hundred different types of antioxidants (i.e., electron- or hydrogen-donating reductants) that may react directly with such reactive oxidants, forming products with much lower reactivity and therefore potentially protecting against oxidative damage [38]. A low adherence to the Med Diet is associated with the development of persistent AF. A study found that, in patients with AF, the prevalent source of antioxidants was coffee, whereas control patients derived more antioxidants from vegetables, fruit and wine [39]. Intake of antioxidants from wine was also lower in patients developing AF. However, patients with low adherence to the Med Diet also had a less healthy lifestyle that could favor the development of arrhythmia, suggesting that multiple mechanisms are involved. In the Mediterranean, alcoholic beverages of all types (mainly wine) are usually consumed with food. It is possible that the antioxidant effects of wine (especially red), combined with the dietary antioxidants of the Med Diet, might have a more beneficial effect on the prevalence of AF, at least in the Mediterranean population. The beneficial effects are related to specific protective chemical polyphenols found in red wine [39,40].

Recently, an association between the Med Diet and heart rate variability (HRV) was suggested [41]. The hypothesis is that the dietary components characteristic of the Med Diet, including food items, nutrients, and diet-related biochemical reactions involving energy generation and nutrient metabolism, may all potentially affect HRV through modulating sympathetic and parasympathetic activity and central thermoregulatory control. The same mechanism has been invoked to understand the impact of caffeine intake on the development of arrhythmias.

Diet & supplements

The Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione trial suggested that fish oil supplements leads to a significant reduction in the risk of SCD among patients with a recent myocardial infarction (MI). The concept that n-3 PUFA may reduce cardiac deaths via antiarrhythmic effects is supported by basic science, animal and human studies. *In vitro* studies have shown that acutely superfused n-3 PUFA can interact with sodium, potassium and calcium ion channels in the cell membrane [42]. Data from Japan eicosapentaenoic acid (EPA) Lipid Intervention Study (JELIS), however, showed that in a group of hypercholesterolemic subjects, high-dose EPA did not confer significant protection against SCD [43]. Similarly, the Study on Omega-3 Fatty Acid and Ventricular Arrhythmia (SOFA) had null results for the n-3 PUFAs [44]. Indirect evidence that ischemia may be a prerequisite for antiarrhythmic effects of n-3 PUFA comes from studies in which patients with an implantable defibrillator were randomized to n-3 PUFA or control [45,46]. The antiarrhythmic effect of fish oil, as demonstrated by the GISSI-prevenzione trial, may

be most profound in the setting of acute ischemia or recent MI. Outside this setting, when ventricular tachycardia occurs as a result of myocardial scar-based re-entry, fish oil may actually increase the risk of ventricular tachycardia or ventricular fibrillation. By contrast, a study carried out on patients with idiopathic dilated cardiomyopathy reported that n-3 PUFAs administration was associated with favorable effects on parameters related to arrhythmic risk suggesting that the antiarrhythmic activity was independent from the anti-ischemic effects [47]. These hypotheses only highlighted the need for further research.

Patients are increasingly using dietary supplements and herbal products for purportedly preventive and therapeutic purposes [48]. Some products have direct effects on the cardiovascular or hemostatic system, whereas others have indirect effects through interactions with medications that could lead to serious consequences [49]. Common herbal remedies that produce adverse effects on the cardiovascular system include St. John's wort, motherwort, ginseng, ginkgo biloba, garlic, grapefruit juice, hawthorn, saw palmetto, danshen, echinacea, tetrandrine, aconite, yohimbine, gynura, licorice and black cohosh. Some of them, that is, oleander, ginkgo and gossypol, could provoke arrhythmias. Some herbal products (aloe vera, bitter orange, echinacea, ginkgo biloba, ginseng, guarana, hawthorn, horny goat weed, licorice, lily of the valley, night-blooming cereus, oleander, rhodiola and St John's wort) induce arrhythmias by prolonging QT interval or interfering with antiarrhythmic drugs [50]. Most (64%) of the patients with a diagnosis of AF or ischemic heart disease reported concomitant use of alternative therapies and prescription drugs [51]. There is a clear need for better public and physician understanding of herbal products through health education, early detection and management of herbal toxicities, scientific scrutiny of their use, and research on their effectiveness and safety [50]. Regulatory policies are also needed to protect people from untoward effects on their health.

Coffee, caffeine & atrial fibrillation

The associations between coffee, caffeine and AF have had conflicting results [52–54]. Caffeine is the most widely consumed behaviorally active substance in the world and almost all comes from dietary sources, most of it from coffee [55]. Caffeine is a nonselective competitive antagonist of adenosine receptor subtypes A1 and A2A in concentrations typically consumed by humans. At higher concentrations, caffeine can induce intracellular calcium release and phosphodiesterase inhibition. Caffeine is an alkaloid that is naturally present in coffee beans; however, it is also present in a number of dietary sources consumed worldwide, in tea, cocoa beverages, chocolate bars, soft drinks and energy drinks.

Studies evaluating the acute effects of caffeine on heart rate found controversial results. After acute ingestion of 100 or 200 mg of caffeine, a significant decrease in heart rate was observed in nonhabitual coffee consumers [56], whether in habitual coffee consumers, the lack of this effect on heart rate depends on rapid tachyphylaxis of caffeine [57]. These results underline the different response in habitual and nonhabitual consumers as

previously reported by authors evaluating hypertensive patients. Different findings were also found in two studies investigating the effects of excessive, toxic caffeine ingestion on HRV [58,59]. Interestingly, the physiologic effects of caffeine differ in men and women. In the Women Health Study, caffeine consumption was not associated with an increased risk of incident AF in initially healthy middle-aged women [60]. The clinical effect of intake of caffeine from coffee, tea and caffeinated soda on AF remains inconclusive. There are some differences among coffee and caffeine intake. Coffee is a complex beverage that includes hundreds of substances including antioxidants. In healthy volunteers the acute ingestion of caffeinated instant coffee does not result in supraventricular arrhythmias [61]. However, many patients with paroxysmal AF indicate coffee intake as a triggering factor for arrhythmia, and there is a fairly widespread belief that caffeine intake is related to the development of AF [62]. In a case–control study we found that increasing levels of coffee consumption were associated with a significantly greater risk of acute AF [63]. High espresso coffee consumption (>three cups/day) was associated with an increased risk of AF, moreover, habitual drinkers had a low probability of spontaneous conversion of the arrhythmia. Caffeine may mediate AF by resulting in neurohormonal stimulation and sympathetic activation and the effects could be enhanced in nonhabitual coffee drinkers [64,65]. As for habitual intake, the FHS and a Danish study showed no association of daily caffeine intake with incident AF [53,66]. Interestingly, a recent incidence of acute stress is associated with an increase in coffee consumption in almost all subjects, habitual and nonhabitual drinkers [67]. Other studies identified moderate coffee consumption (one to four cups/day) as a contributor to AF risk [68], whereas another study showed that caffeine was associated with less successful cardioversion in participants with hypertension [35]. It is plausible that the effect of caffeine varies in habitual versus nonhabitual consumers and also depends on the dose, on the modality of preparation and on the modality of intake, for example, coffee after meals. Further studies are needed to clarify the relation of caffeine exposure to risk of incident and recurrent AF in healthy individuals and in patients with a predisposition for AF.

Alcohol & atrial fibrillation

An interesting analysis was carried out on the association of modifiable factors, such as coffee intake, cigarette smoking, alcohol consumption and physical activity with QT interval duration [69]. In the large sample representative of the general US population, the authors found no association between QT interval duration and coffee or tea intake, cigarette smoking, physical activity, or total alcohol intake, although binge drinking was associated with an increased QT duration, particularly in men.

Several studies have identified a variety of ECG abnormalities, including prolonged QT interval in chronic alcoholics or heavy drinkers. Abnormalities of electrolytes, increased sympathetic tone and catecholamine secretion, as well as cardiac cellular infiltrate, hypertrophy and fibrosis are frequently seen in chronic alcoholism, which may all cause changes in QT interval [70–72].

Electromechanical experiments also suggest a concentration dependent effect of alcohol on action potential duration, with a decreased duration of repolarization at very high concentrations of alcohol but no effect at low concentrations [73].

The proarrhythmic effects of ethanol are controversial and strongly dependent on the amount of alcohol consumed and the pattern of drinking. Excessive alcohol intake increases the risks of motor vehicle accidents, stroke, cardiomyopathy, cardiac dysrhythmia and SCD [74]. Acute alcohol intake and binge drinking have been related to AF [75], whereas, moderate alcohol intake was not associated with a higher risk of SCD [76]. Moderate alcohol consumption may lower the risk of some cardiovascular diseases but the association with arrhythmic disorders is less clear. Epidemiologic data of the long-term relation of alcohol intake have been inconsistent. Data from the Cardiovascular Health Study showed no effect of alcohol intake on AF [77], whereas the FHS study found that moderate-to-heavy alcohol consumption (more than three drinks/day; 36 g alcohol) is significantly associated with increased AF risk in men [78]. A similar association has been identified in women, where the consumption of more than two drinks/day (equivalent to 25 g alcohol/day) increased AF risk [79]. Recently, it has been hypothesized that not only episodic but also habitual heavy alcohol consumption is associated with the risk of AF [80]. The arrhythmogenicity of chronic alcohol exposure may stem from alcoholic cardiomyopathy, increased oxidative stress, neurohormonal activation and altered calcium homeostasis [81,82].

A recent meta-analysis of 14 studies, evaluating the relationship between AF and alcohol, concluded that habitual heavy alcohol drinking is associated with an increased risk of AF, although several study limitations exist and must be recognized [83]. The relationship between daily alcohol consumption and the risk of AF was explained by a linear dose-response model, suggesting that not consuming alcohol at all is the most favorable behavior for avoiding AF, rather than moderate alcohol consumption.

Similarly, the healthy effects of alcohol intake are also controversial and strongly depend on dose and modality of intake [84]. In the analysis of nine nationally representative samples of the US population, comprising over 10,000 cardiovascular deaths, light and moderate alcohol consumption was associated with lower cardiovascular mortality, whereas heavy alcohol consumption was not [85]. The magnitude of lower risk was generally strongest for coronary heart disease mortality and among non-Hispanic whites. These data support previous epidemiological studies that have found lower rates of CVD among moderate drinkers [86,87]. Most studies report J-shaped curves, whereby light-to-moderate drinkers have less risk of CV events than abstainers, and heavy drinkers are at the highest risk [88–90]. A recent meta-analysis of 12,819 patients with CVD showed that light-to-moderate alcohol consumption (5–25 g/day) was significantly associated with a lower incidence of cardiovascular and all-cause mortality [91].

Mechanisms supporting antiatherosclerotic effects of moderate intake of alcohol include beneficial regulation of lipids

and fibrinolysis, decreased platelet aggregation and coagulation factors, beneficial effects on endothelial function, and inflammation and insulin resistance [92].

Moreover, in the Mediterranean alcohol, mainly wine, is mostly consumed during meals, and reports now suggest that wines contain antioxidant compounds and may modulate the health effects of other nutritional compounds in the stomach [92,93].

Expert commentary & five-year view

Despite great progress and success in the improvement of cardiovascular outcomes, the gains of recent years are likely to be overshadowed by the sheer volume of CVD that will accrue from untreated risk factors. The greatest health gains could come from preventive strategies. One example of such an approach is the 2010 Dietary Guidelines for Americans which recommend balancing of calories, reduction of salt and decrease of cholesterol intake. Healthy lifestyle influences the development of arrhythmias and is strongly related to AF development.

Atrial fibrillation is the most frequent arrhythmia in clinical practice and its prevalence is growing. The majority of patients with AF had a structural cardiac disease; however, a small number of them had no morphological modification of the heart. The impact of a nonhealthy lifestyle on the development of AF strongly depends on the relationship between the obesity and cardiac chamber changes leading to atrial dilation and AF. Furthermore, some 'nonhealthy' habits could directly influence the development of arrhythmias. Coffee, caffeine and alcohol demonstrated different effects on AF, mainly related to the global lifestyle of subjects. Coffee and caffeine intake has effects on AF according to the modality of preparation, the daily quantity of caffeine and the relationship with other food. Adherence to the Med Diet strongly influenced the outcome of cardiac disease and, similarly, the intake of coffee and alcohol within a healthy diet seems to contribute to a good bioavailability of antioxidants and anti-inflammatory food.

The controversial data emerging from clinical trials are mainly due to selection criteria and are affected by the difficulties of collecting data on food intake and, in particular, on alcohol intake. A healthy lifestyle is associated with a reduction of CV events through weight control and visceral adiposity control. The beneficial effect on AF is related to the reduction of structural cardiac disease, the reduction of atherosclerosis and of atrial and ventricular dysfunction. Referring to the recent guidelines we emphasize the importance of education and the influence of communities to enable and encourage healthy choices.

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Key issues

- The relationship between lifestyle and atrial fibrillation (AF) has not been fully explored.
- Data from different studies are controversial.
- General opinion states that a healthy lifestyle reduces cardiovascular risk.
- A healthy lifestyle could act positively on AF, secondary to cardiac disease, by reducing the impact of obesity and metabolic syndrome leading to cardiac abnormalities.
- The balance between a healthy diet and moderate intake of coffee and alcohol could positively affect the development of AF in patients with no structural disease.

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