

Review Article

The Effect of Diet on Cardiovascular Diseases: Cardiac Arrhythmias Part I

Abstract

The heart is a mechanical pump, and it contracts in response to a bioelectrical signal, the action potential. The action potential originates in the sinus node cells, spreads through both atria, causing their contraction. The next stage of propagation is the atrioventricular (AV) node, which passes the signal to the ventricles with a slight delay to provide enough time for the atria to contract. From the AV node, the bundle of His conducts the stimulus along the septal wall to the subendocardial Purkinje fibers, which then stimulate the ventricles, allowing their synchronized contraction. Disturbances of action potential generation and/or conduction can lead to changes in the regular heart rhythm called arrhythmias. Cardiac arrhythmias are usually due to cardiovascular diseases. Diet impacts cardiac arrhythmias by reducing cardiovascular diseases. However, diet can also directly influence arrhythmia incidence and severity. The influence of diet as a low-cost intervention to improve cardiovascular health and reduce cardiac arrhythmias is discussed in this 2-part manuscript.

Keywords: cardiac arrhythmias, fruits and vegetables, nuts, whole grains, fish, coffee, chocolate

Introduction

Cardiac arrhythmia, also called cardiac dysrhythmia, is defined as any change from the normal sequence of electrical impulses. Although usually caused by cardiovascular ailments, cardiac arrhythmias themselves can lead to major cardiac complications, such as heart failure, stroke, or cardiac arrest¹. The two major arrhythmias of concern are atrial fibrillation (AF) and malignant ventricular arrhythmias. Atrial fibrillation is the most common arrhythmia encountered in clinical practice^{2,3}. It is estimated that by 2030, 14 to 17 million people in Europe, and 12.1 million people in the United States will be diagnosed with AF^{3,4}. Atrial fibrillation predisposes to major morbidities, including ischemic stroke, other systemic embolisms, dementia, heart failure, myocardial infarction, and chronic kidney disease^{5,6}. It also results in functional limitations, increased disability, and diminished quality of life⁷. The cardiovascular death rate is increased⁸. Its presence also increases overall mortality⁹. According to the US Centers for Disease Control and Prevention (CDC), AF was the underlying cause of death in 26,535 individuals in 2019 (in the USA)¹⁰. The overall healthcare use increases and the costs go up¹¹. The underlying mechanism is usually ectopic foci and reentry in the atrial tissue¹².

The second clinically important arrhythmia is malignant ventricular arrhythmias. These usually occur in the setting of structural heart diseases such as myocardial infarction, dilated non-ischemic cardiomyopathy, and cardiac sarcoidosis¹³. They are most often seen with ischemic heart events¹⁴ and invariably result in deleterious hemodynamic complications¹⁵. These are also tied to a feared outcome - sudden cardiac death (SCD)¹³. Death attributable to cardiac causes and

occurring within 1 hour of the onset of symptoms is defined as SCD¹⁶. Coronary heart disease (CHD) is responsible for almost 80% of cases of SCD, and SCD may, unfortunately, occur as its first manifestation¹⁷. Sudden cardiac death accounts for about 1 in 7.5 deaths in the United States¹⁸. SCD results from the occurrence of asystole and pulseless electrical activity or sustained ventricular arrhythmias, such as ventricular tachycardia and fibrillation¹⁹. Idiopathic ventricular arrhythmias, usually PVCs, although less ominous, may occur in normal hearts. In this population, they tend to occur in approximately 40% of adults on 24-h Holter monitoring²⁰. Ventricular arrhythmias result from several mechanisms – the three most common are abnormal automaticity, triggered activity, and reentry^{21,22}. Current guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden death have been published in 2015 by the European Society of Cardiology²³ and in 2017 by the American Heart Association (AHA)/American College of Cardiology/Heart Rhythm Society¹³.

Cardiac arrhythmias arise due to enhanced or abnormal impulse generation (focal activity) and conduction disturbances (re-entry)^{24,25}. As mentioned above, underlying cardiac disease is by far the main substrate for these mechanisms and the development of AF and SCD. Other influences implicated include cardiotoxin exposure, medication side effects, cigarette smoke, stress, and the use of stimulant drugs²⁶⁻³⁰. Adherence to a low-risk lifestyle is associated with a low risk of AF and SCD³¹. Diet also plays an important role in both the primary prevention and secondary prevention of both arrhythmias, mainly by mitigating against structural heart disease³². The role of dietary components and supplements on the development and progression of AF and ventricular arrhythmias are discussed in this manuscript.

Discussion

Lifestyles play an important role in human morbidity and mortality. The AHA Strategic Planning Task Force and Statistics Committee suggested an ideal cardiovascular lifestyle can be achieved by monitoring seven simple parameters, conveniently called the Life's Simple 7 (LS7)³³. These consist of 7 modifiable health behaviors and biological factors (smoking, body mass index [BMI], physical activity, diet, total cholesterol, blood pressure, and fasting blood glucose). It is estimated that LS7 compliance can improve cardiovascular health by 37%. The LS7 compliance also has an impact on AF – it portends a 57% lower risk³³.

Alcohol intake is not included in LS7. Traditionally, the accepted notion is that intake of low to moderate levels of alcohol is cardiovascular protective³⁴. However, recent data suggests that even a single drink of alcohol may not be safe for overall health^{35,36}. Wood et al analyzed 600,000 individuals and found that more than 1 drink a day increased all-cause mortality³⁵. Griswold et al. in 2018, in a systematic review and meta-regression analysis (28 million individuals aged 15 to 49 years) reported that the lowest health loss was seen in individuals that had zero standard drinks per week³⁶. A recent brief from the World Heart Federation warned against the dangers of alcohol and proclaimed that 'any level of alcohol consumption can lead to loss of healthy life'³⁷. Despite this alcohol-related data, there is ample evidence that following healthy lifestyles (including low to moderate intake of alcohol) provides significant health benefits^{38,39}. Li et al. estimated that the life expectancy at age 50 years was 29.0 years for women

and 25.5 years for men who adopted zero low-risk lifestyle factors. In contrast, for those who adopted all 5 low-risk factors, the projected life expectancy at age 50 years was 43.1 years for women (a gain of 14 years) and 37.6 years for men (a gain of 12.2 years)³⁸. This manuscript deals with the role of one of these lifestyle factors, namely diet, in the pathogenesis of cardiac arrhythmias³³. Diet can influence these in two ways – by increasing body weight and by the individual actions of its ingredients.

Quantity of calories consumed

A body mass index (BMI) is commonly used to assign a bodyweight category in humans. A BMI ideally should be 18.5 kg/m² to 24.9 kg/m². A BMI between 25 kg/m² to 29.9 kg/m² is considered overweight, while at or >30 kg/m² is consistent with obesity³⁹. Proper intake of foods and beverages is crucial for a healthy body weight⁴⁰. This means that the balance between energy intake (calories taken in) and expenditure (calories burned) may need to be adjusted if the bodyweight is not ideal^{41,42}. A BMI between 18.5 kg/m² and 24.9 kg/m², once achieved, can be maintained by combining a healthy dietary pattern and with ≥ 150 minutes of moderate physical activity per week⁴³. In general, metabolic needs decrease by about 70-100 calories per day with each decade of adult life. Obesity has adverse effects on cardiac structure and function, leading to an increased risk of several cardiovascular diseases (CVDs) including hypertension, CHD, and heart failure (HF)⁴⁴. As mentioned before, underlying heart disease is a major risk factor for AF⁴⁵ and SCD⁴⁶.

Several observational cohort studies have highlighted obesity as an independent risk factor for the development of AF⁴⁷⁻⁵⁰. The ARIC (Atherosclerosis Risk In Communities) study estimated that almost 1 in 5 cases of AF could be attributable to overweight or obesity⁵¹. Wang et al calculated that there was a 4.7% increase in the risk of AF with each kg/m² rise in BMI⁵². Obesity also affects AF prognosis. Winkle et al observed a significantly higher risk of complications in AF patients with BMI ≥ 40 kg/m²⁵³, Shoemaker et al reported in their prospective study that BMI ≥ 40 kg/m² was associated with a greater risk of complications even after AF ablation⁵⁴.

Weight loss helps. Pathak et al. demonstrated that AF patients with significant intentional weight loss over a 5-year follow-up (>10%) had a 6-fold higher likelihood of arrhythmia-free survival, as compared with those with modest- to no-weight change (<3%)⁵⁵. Increasing evidence indicates that obesity may contribute to the AF through several pathways such as increasing left atrial volume⁵⁶ and left atrial fibrosis^{57,58}. There is also an upregulation of inflammatory markers in these patients⁵⁹.

Obesity is also associated with malignant ventricular arrhythmias and SCD⁶⁰. The QT interval (on the surface electrocardiogram) represents the time from onset of ventricular depolarization to completion of repolarization. This interval, if prolonged (QTc value >450 ms in males and >460 ms in females, measured preferably in lead II or V5 on a standard 12-lead ECG), encourages ventricular arrhythmias and these may trigger torsades de pointes, ventricular fibrillation, and sudden cardiac death^{61,62}. Significant prolongation of QT (or QTc) is often seen in overweight and obese patients⁶³. Sabbag et al. and Vink et al. found that each 1 kg/m² increase in BMI was

associated with a significant 4% increased adjusted risk for exercise-induced ventricular arrhythmias^{64,65}. The QTc is appreciably decreased with a substantial weight loss^{66,67}. Obesity in patients with malignant ventricular arrhythmias is associated with increased left ventricular (LV) diameter and mass⁶⁸, concentric LV hypertrophy⁶⁹, LV diastolic dysfunction⁷⁰, and fibrosis⁷¹. They also have repolarization abnormalities⁷². All these changes promote SCD.

Besides the quantitative risk of diet, the quality of diet also affects cardiac arrhythmias, especially by influencing the risk and progression of cardiovascular diseases.

Fruits and Vegetables

Fruits and vegetables have been associated with a benefit in virtually all CVDs^{73,74}. They provide potassium – low potassium in the serum is associated with an increase in the risk of lethal ventricular arrhythmias in patients with CVD. Potassium supplements tend to reduce blood pressure⁷⁵. It is well known that higher consumption of fruits and vegetables helps prevent potassium deficiency⁷⁶. Studies also suggest that high consumption of fruit and vegetables also reduces sympathetic and enhances parasympathetic activity, and this may help prevent SCD and arrhythmia^{77,78}. Grapefruit juice may markedly increase dronedarone HCl blood levels if taken in combination with the drug, resulting in excessive prolongation of the corrected QT interval, and resulting in ventricular arrhythmias, including torsade de pointes and cardiac arrest in clinical practice^{79,80}. Caution, therefore, needs to be exercised with imbibing grapefruit juice in patients who are on dronedarone.

Nuts

Ingestion of nuts is CVD protective. Larsson et al. reported from a large prospective study that nut consumption may play a role in reducing the risk of AF. In their study of 61,364 Swedish adults (followed for up to 17 years), data showed that the hazard ratio for AF was 0.97 for nut consumption 1-3 times/month, 0.88 for nut consumption 1-2 times/week, and 0.82 for nut consumption ≥ 3 times/week⁸¹. In this study, there was an 18% reduction in the risk of AF in those who consumed nuts ≥ 3 times/week. Consumption of nuts has been associated with improved serum cholesterol⁸², lower blood pressure⁸³, weight loss⁸⁴, decreased risk of diabetes⁸⁵, a lower incidence of ischemic heart disease⁸⁶, and a reduced risk of cardiovascular mortality⁸⁷. Nuts may beneficially influence cardiovascular health through their anti-inflammatory and antioxidant effects⁸⁸, and their role in improving endothelial function⁸⁹.

Nuts also appear to protect against malignant ventricular arrhythmias. Albert et al. reported that individuals in the US Physicians Health Study, who consumed nuts 2 or more times per week had a 57% reduced risk of SCD when compared with men who rarely or never consumed nuts. This reduction was noted even after controlling for known cardiac risk factors and other dietary factors. They found that the risk of SCD was 47% lower in men who consumed nuts ≥ 2 times per week compared with men who rarely or never consumed nuts⁹⁰.

Whole grains/fiber

The consumption of whole-grains and dietary fiber, especially cereal fiber, reduces CVD morbidity and mortality⁹¹⁻⁹³. The fiber, vitamins, minerals, and various phytochemicals in whole-

grains⁹⁴ decrease inflammation and oxidative stress⁹⁵. Inflammation and oxidative stress play a role in the pathophysiology of AF⁹⁶. Whole-grains are also a good source of dietary magnesium, and this may provide additional protection against AF⁹⁷. The specific benefit of whole grain intake on malignant ventricular arrhythmias is scarce, but diets such as the Mediterranean (see Part II), are rich in whole-grains and have a beneficial effect in protecting against SCD⁹⁸.

Fish

The omega-3 fatty acids, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are present in fish and marine products, with the highest concentrations in fish oils⁹⁹. These have been linked to a reduction in CVDs^{100,101}. Studies on fish oil intake in elderly patients have reported a reduced risk of developing AF¹⁰². Subsequent studies have, however, not supported this finding. A large-scale randomized study revealed no reduction in the incidence of postoperative AF with fish oil supplementation¹⁰³. A meta-analysis of published studies, by Mariani et al., found that fish oil and omega-3 polyunsaturated fatty acids (PUFA) intake had no AF protective effects¹⁰⁴. The effects of fish oil intake in preventing postoperative AF and in the secondary prevention of AF, therefore, remains unclear.

Their benefits in protecting against malignant ventricular arrhythmias are however clearer¹⁰⁵. Fish consumption was inversely associated with the risk of SCD in the Physicians' Health Study, with an apparent threshold effect at a consumption level of 1 fish meal per week¹⁰⁶. Consumption of fatty (higher EPA and DHA levels), but not lean fish was inversely associated with risk of SCD in the Zutphen Study¹⁰⁷. Both α -linolenic acid and marine n-3 fatty acids (EPA and DHA) were significantly inversely associated with the risk of SCD in the Nurses' Health Study^{108,109}. Albert et al and others have shown that increased consumption of fatty fish and n-3 PUFA appear to decrease the risk of SCD¹¹⁰⁻¹¹⁴, by reducing ventricular fibrillation¹¹². Their protective effects have also been seen in patients with implanted cardiac defibrillators (ICDs). In one study, ingestion of four 1 gm. capsules of n-3 PUFA was associated with a longer time to first ICD events and an overall decreased risk of having an ICD event¹¹⁵. Increased consumption of dark oily fish and n-3 PUFA, therefore, appear to decrease the risk of malignant ventricular arrhythmias and SCD^{112,113,116,117}. The AHA recommends consumption of two servings of fish per week (or supplementation with 1 g/day of EPA and DHA) for persons with no history of coronary heart disease and at least one serving of fish daily for those with known coronary heart disease¹¹⁸. A word of caution though - fish eaten (twice a week) should be low in environmental contaminants such as methyl mercury, polychlorinated biphenyls, and dioxins. Fish typically high in these include - shark, swordfish, king mackerel, or tilefish (golden bass and golden snapper) and their intake should be minimized¹¹⁹. High-quality fish oil supplements usually do not contain these contaminants. Although omega-3 PUFA, are mainly found in fish and marine products, they can also be theoretically obtained from vegetable sources¹²⁰. Alpha-linoleic acid (ALA) present in certain vegetables (e.g., hemp, flax, walnut, and algae) is slowly metabolized to long-chain polyunsaturated ω -3 fatty acids¹²¹. However, this conversion into EPA and DHA is very limited, and clinical impact is probably very low.

Coffee/Tea/Energy Drinks

It is now well accepted that a consumption of 3-5 cups of coffee a day is associated with a lower risk of incident CHD and stroke¹²². Intake is also associated with a reduced CVD mortality¹²³ and all-cause mortality¹²⁴. In the past, it was postulated that coffee may be proarrhythmic because of its neurohormonal stimulation and sympathetic activation properties¹²⁵⁻¹²⁷. Several earlier studies had reported that acute and chronic coffee consumption contributed to the development of AF^{128,129}. Coffee was implicated in leading to less successful cardioversion in patients with hypertension¹³⁰. However, subsequent studies show that habitual intake of coffee is not related to incident AF¹³¹. On the contrary, recent studies suggest that coffee intake has a protective effect on AF¹³². Population-based studies have consistently demonstrated a reduction in AF with increasing levels of caffeine ingestion. Incident AF events in 57,053 participants followed for 13.5 years were lower in habitual coffee drinkers at all levels of consumption (Hazard Ratio or HR= 0.79 for 6 to 7 cups per day)¹³³. A meta-analysis of 6 prospective cohort studies with 228,465 participants similarly demonstrated an inverse relationship, with AF incidence decreasing by 6% for every 300 mg/day increment in regular caffeine intake¹³⁴. In a further meta-analysis of 115,993 patients, Caldeira et al. found that pooled results were consistent with a significant 13% reduction in incident AF risk¹³⁵. Klatsky et al. studied a population of 130,054 people and found that 3,137 subjects (2.4%) were hospitalized for arrhythmia over a 17.6 years' follow-up. In this study, caffeine intake was also inversely related to arrhythmia risk (including AF risk)¹³⁶. Most recent studies continue to corroborate the beneficial effects of coffee drinking on atrial arrhythmias. A recent study, published in 2019 in the Journal of the AHA, of men in the US Physicians' Health Study (N=18,960) suggested a lower risk of AF with consumption of 1 to 3 cups/day¹³⁷. An even more recent study (18,983 and 6,479 participants from the 'Seguimiento Universidad de Navarra' (SUN) and 'Prevención con Dieta Mediterranean' (PREDIMED) cohorts) respectively, found that intermediate levels of caffeinated coffee consumption (1-7 cups/week) reduced AF risk¹³⁸. In a prospective cohort study, Mendelian randomization failed to provide evidence that caffeine consumption increased arrhythmia risk. This study also showed that each additional cup of habitual coffee consumed was associated with a 3% lower risk of incident arrhythmia (HR= 0.97)¹³⁹. Coffee intake may also protect against ventricular arrhythmias – or at least may not be harmful. Although many earlier reports suggested a detrimental effect of coffee on these, it appears that animal studies were based on intake of very high doses of caffeine¹⁴⁰. In humans, consumption of about 400 mg a day or about 5 cups of coffee a day appears to be associated with no increase in ventricular arrhythmias. However, episodic coffee consumption has been known to trigger SCD¹⁴¹. Tea consumption appears to reduce both atrial arrhythmias and ventricular arrhythmias¹⁴². In a meta-analysis, Zhang et al. found that consumption of 3 cups of tea per day significantly reduced the risk of cardiac death (relative risk 0.74)¹⁴³. Energy drinks may contain caffeine in significantly higher concentrations than in coffee and tea and may show pro-arrhythmogenic effects (both atrial and ventricular arrhythmias) in individuals with normal structural hearts¹⁴⁴.

Chocolate

Chocolate consumption appears to be associated with a decreased risk of AF. Data from the Women's Health Study showed that moderate chocolate intake was associated with a 1%–14% lower rate of self-reported AF^{145,146}. More recently, Larsson et al. in a review of studies that

included 180,454 participants and 16,356 AF cases, found that the hazard ratio was 0.97 per 2 servings/week increase in chocolate consumption and 0.96 for the highest versus lowest category of chocolate consumption¹⁴⁷. Inflammation plays a role in the development of AF and chocolate has anti-inflammatory actions¹⁴⁸. Further, chocolate also provides magnesium (100 calorie serving of dark chocolate contains 36 mg of magnesium) and this may also help in producing an antiarrhythmic effect¹⁴⁹. Chocolate intake has been known to protect against CVDs, and although no reliable study on chocolate use and ventricular arrhythmias could be found, it is tempting to associate its consumption with a lower incidence of SCD.

Conclusion

Diet can play a significant role in decreasing the risk of CVD, including cardiac arrhythmias. Atrial fibrillation is a common atrial arrhythmia. It is the major cause of embolic stroke. Diet plays a significant role in preventing obesity, which is negatively associated with both serious atrial and malignant ventricular arrhythmias. A plant-based diet rich in fruits, vegetables, nuts, whole grains decreases the risk of AF. The data on fish intake and AF is unclear. Chocolate, coffee, and tea in moderate amounts appear to be beneficial. Energy drinks may however have significantly larger amount of caffeine, and this may make them arrhythmogenic. As far as malignant ventricular arrhythmias are concerned, a diet that helps prevent AF also appears to mitigate ventricular arrhythmias. The role of fish intake is more persuasive in its effects on the latter. The beneficial effects are primarily due to omega 3 PUFAs in fish. The role of chocolate is unclear while excessive caffeine intake via energy drinks may be harmful to ventricular arrhythmias. Part II of this manuscript discusses the role of red meat, alcohol, micronutrients, and some common diets on cardiac arrhythmias.

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