Review Article

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

Abstract

Cardiac arrhythmias are common in clinical practice. The two most common are atrial fibrillation and malignant ventricular arrhythmias leading to sudden cardiac death. As noted in part I of this two-part manuscript, a plant-based diet, and fish intake appear to reduce the incidence of these troublesome arrhythmias. In this part II, the effect of alcohol, red meat, saturated fat, certain electrolytes and minerals, and commonly prescribed diets for cardiovascular protection, is discussed.

Keywords: cardiac arrhythmias, alcohol, red meat, saturated fats, diet

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia1. It is estimated that people have a 25% lifetime risk of developing AF[1]. AF is commonly seen in patients with structural heart disease such as heart failure, hypertension, valvular disease, and myocardial infarction[2]. These are usually associated with atrial fibrosis, making the atrial tissue a proarrhythmic substrate for atrial foci to develop abnormal automaticity, self-sustaining action potentials, or re-entrant circuits[3]. AF may be triggered by hypokalemia, hypomagnesemia, hypovolemia, and alterations in parasympathetic and sympathetic activity[4]. Atrial fibrillation is not benign. It increases the risk of ischemic stroke 5-fold, and stroke is a leading long-term disability and death[5]. AF also increases hospitalization and mortality from ischemic heart disease and heart failure6. It is also associated with an increase in all-cause mortality[7]. Besides attempts to convert to normal sinus rhythm with drugs like flaicanamide medicines (beta-blockers and calcium channel blockers) to control the heart rate, patients with AF also receive oral anticoagulation therapy to prevent future thromboembolic events[8]. Catheter ablation is also increasingly being used to convert these patients to sinus rhythm[9]. However, relapses may occur in up to 30% of patients. AF is associated with a substantial economic burden[10]. The second most important rhythm disturbance is associated with sudden cardiac death (SCD)[11]. The World Health Organization (WHO) defines SCD as a sudden unexpected death within 1 hour of symptom onset or within 24 hours of having been last seen well[12.] The cause for the fatal cardiac arrest is usually a malignant ventricular arrhtymia[13] - a ventricular tachycardia that degenerates into ventricular fibrillation[14,15]. In up to half of SCDs, the fatal event is the first indication that the patient had cardiovascular disease (CVD)[16]. Coronary heart disease is commonly the underlying CVD[17]. The estimated global survival rate of sudden cardiac arrest is less than 1%[18]. Part I looked at the effect of fruits, vegetables, nuts, whole grains, tea, coffee, chocolate, energy drinks, and fish intake on these arrhythmias. This Part will discuss the impact of the intake of red meat, saturated fat, alcohol, micronutrients, and special diets on AF and SCD.

Discussion

The American Heart Association Strategic Planning Task Force and Statistics Committee suggested monitoring seven simple parameters namely smoking, body mass index (BMI), physical activity, diet, total cholesterol, blood pressure, and fasting blood glucose[19]. These five if kept to ideal levels provide excellent cardiovascular protection. According to AHA, a 1-point-higher Life's Simple 7 (LS7) score provides an 11% lower risk of incident AF. Alcohol intake was not included in this LS7. Traditionally, intake of low to moderate levels of alcohol has been considered cardiovascular protective[20]. However, recent data suggests that not a single drink of alcohol is safe. Wood et al analyzed 600,000 individuals and found that even 1 drink a day increased all-cause mortality[21]. Griswold et al. in a systematic review and meta-regression analysis (28 million individuals aged 15 to 49 years) in 2018, reported that the lowest health loss was seen in individuals that had zero standard drinks per week[22]. 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'[23]. Despite this data, there is ample prevailing evidence that following five healthy lifestyles (not smoking, maintaining ideal body weight, not drinking alcohol, or drinking alcohol in low to moderate amounts, exercising regularly, and eating a prudent diet) provides significant benefits. 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)[24].

Red meat /Saturated fat/trans-fat/refined carbohydrates

Red meat and processed red meat consumption have a direct association with CVD incidence and mortality[25]. A prospective study of 409,885 men and women in nine European countries showed a similar increase in the risk of coronary heart disease (CHD) for every 100 g/day increments in the intake of total and processed red meat. Substituting 100 kcal/day of fatty fish, yogurt, cheese, or eggs for 100 kcal/d of red and processed meat is associated with a 15-24% lower risk of ischemic heart disease[26]. In a recent prospective cohort study of men with at least 30 years of follow-up, greater intakes of total, unprocessed, and processed red meat were associated with a higher risk of CHD risk[27]. The hazard ratio (HR) in this study, for one serving per day increment, was 1.12 for total red meat, 1.11 for unprocessed red meat, and 1.15 for processed red meat after a multivariate adjustment for dietary and non-dietary risk factors. Processed red meat appears to be more dangerous for CAD. Micha et al. reported that a review of incident CHD based on six studies including 614,062 participants and 21,308 events indicated that each 50 g serving/day of processed meat was associated with a 42% higher risk of CHD[28]. They specifically increase the risk of myocardial infarction, stroke, and heart failure – all of which are arrhythmogenic[29-31]. These usually occur due to autonomic imbalance after an MI causing enhanced automaticity of the myocardium and conduction system[32,33]. These patients may also have electrolyte imbalances (such as hypokalemia and hypomagnesemia) and hypoxia which may also contribute to the development of cardiac arrhythmia. The damaged myocardium acts as a substrate for re-entrant circuits, due to changes in tissue refractoriness[34-36]. The

deleterious link between the consumption of processed and unprocessed red meat and the risk of stroke is significant. Kim et al. found that pooled relative risks were increased for red meat consumption and stroke incidence, being 1.11 for red meat intake and 1.17 for processed meat intake[37]. Tong et al. analyzed the data of 418,329 men and women from nine European countries (12.7 years of follow-up) and reported a higher risk of stroke with higher red meat consumption[38]. Cardiac arrhythmias are highly prevalent during the acute phase of stroke and may harm patients by hemodynamic instability and sudden cardiac death[39]. In addition to arrhythmias because of cardiac comorbidities, neuro-cardiological interactions and autonomic dysfunction may complicate the course of cerebrovascular disorders[40,41]. The highest risk for arrhythmia onset was evident within the first 24 hours after admission, during which 74% of all events occurred[42]. Patients after acute stroke have an increased risk for SCD. In these cases, ventricular fibrillation or pulseless ventricular tachycardia are the leading causes of cardiac arrest[43,44]. Other arrhythmias are less common and less life-threatening[45]. Stroke patients have an impairment of cardiovascular autonomic control, indicated by a loss of overall autonomic modulation, lower parasympathetic tone, impaired baroreflex sensitivity, and a shift toward sympathetic dominance[46].

Heart failure is also higher in patients eating unprocessed red meat. In a cohort of 37,035 Swedish men, the consumption of unprocessed red meat was not associated with an increased risk of heart failure (HeF) (HR=0.99 with a median intake of 83.2 g/day vs.17 g/day) or HF mortality[47]. However, the consumption of processed meat was associated with an increased risk of HeF - for each 50 g per day increment in intake, the risk of HeF increased by 8% (HR=1.08), and HeF mortality increased by 38% (HR=1.38). In women (cohort of 34,057 Swedish women, 2,806 of whom were diagnosed with HeF during 13 years of follow-up) Kaluza et al. reported similar findings. For each 50 g day−1 increase in processed red meat consumption, the risk of HeF in women increased by 11%-19%[48]. AF occurs in over half of all patients with HeF[49]. Heart failure contributes to the development of AF via multiple mechanisms. It increases atrial filling pressure and atrial dilatation, leading to atrial scarring and fibrosis, promoting ionic remodeling and AF[50]. Atrial tissue stretching in HeF promotes AF by inducing triggered activity[51]. Left atrial dilatation has been shown in animal studies to be associated with significant shortening of the atrial refractory period, which has been shown to promote AF[52,53].

Trans fats increase systemic inflammation as well as brain natriuretic peptide levels in HeF patients[54]. Fried foods are high in saturated fats and have trans fats. In a large prospective study of 15,362 male physicians, there was a major increase in HeF risk in those with the highest versus the lowest levels of fried food consumption[55].

Low-fat or fat-free dairy products instead of full-fat dairy products: Dietary patterns that include low-fat dairy are associated with a lower risk of obesity, CVD, and mortality. Liquid plant oils rather than tropical oils (coconut, palm, and palm kernel), animal fats (e.g., butter and lard), and partially hydrogenated fats are healthier. Liquid plant oils are rich in unsaturated fats, which reduce low-density lipoprotein (LDL) cholesterol and CVD risk, as are peanuts, most tree nuts, and flax seeds[56]. High intake of ultra-processed foods is associated with obesity, type 2 diabetes, CVD, and all-cause mortality[56]. In mice, high-fat diet increases the vulnerability to atrial

arrhythmia by down-regulation of Cx40 via miR-27b, rather than fibrosis, which is independent of inflammation[57]. The role of these in the prevention of CAD, stroke, and heart failure has been discussed before[58]. There is evidence that high levels of trans-18:2 in red blood cell membranes are associated with a markedly higher risk of SCD. While further studies are needed to investigate the possible effects of trans-18:2 on arrhythmia, it would be prudent to limit dietary intake of trans-18:2[59].

Sudden cardiac death, also known as out-of-hospital SCD, is the leading cause of death from coronary heart disease[60]. The prevention of SCD in the community remains a challenge[61]. There is strong evidence from epidemiologic studies and clinical trials that dietary intake of long-chain n-3 polyunsaturated fatty acids from seafood reduces the risk of SCD[62]. Among persons without prior clinical coronary disease, both dietary long-chain n-3s and membrane or whole blood levels of these fatty acids are consistently associated with a lower risk of SCD[63,64].

Alcohol

Alcohol intake has a complex relationship with cardiac arrhythmias. The association between alcohol intake and AF has been considerably evaluated. The benefit of light or moderate alcohol intake on AF is unclear. It has been suggested that low doses of red wine (due to its resveratrol content) may be arrhythmia protective, but clinical trials are lacking[65]. Excessive alcohol intake is a well-known risk factor for AF, both acutely and chronically. Binge drinking (males = consumption of ≥ 5 standard drinks and females = ≥ 4 standard drinks during one sitting) may lead to the "Holiday Heart Syndrome" – or the occurrence of supraventricular arrhythmias, including AF. Reports have also indicated that binge drinking may also be associated occasionally with frequent ventricular premature beats and rarely, ventricular tachycardia[66,67]. The pathophysiology behind AF onset after binge drinking is not entirely clear and is likely multifactorial, encompassing direct (cytotoxic) and indirect (increased sympathetic and parasympathetic activity) mechanisms. Djousse et al. reported that moderate-to-heavy chronic alcohol consumption (≥3 drinks/d; ≈36 g alcohol) was significantly associated with increased AF risk in men[68]. This was confirmed in the Framingham Heart Study, which revealed a significant association between moderate-to-heavy alcohol intake and increased AF risk in men[69]. The association with excess alcohol consumption (≥2 drinks/day or >25 g alcohol/day) and AF risk has also been noted in women[70]. Several subsequent studies have confirmed this association between higher levels of alcohol intake and incident AF[66,71-73]. A problematic pattern of alcohol use leads to alcohol use disorder (AUD)[74]. These individuals demonstrate significant distress or impairment. According to the American Psychological Association, these patients should meet at least two of the 11 diagnostic criteria presented in DSM5[75]. Past studies have found a strong association between AUD and cardiac arrhythmias. Moderate drinkers have an incidence rate of 17.3% for cardiac arrhythmias, while heavy drinkers (such as those suffering from AUD) have an incidence rate of 20.8% per 1,000 persons-years[76.] Studies show that there is an increase of 8% relative risk of incidence of arrhythmia for each drink per day in heavy drinkers when compared to non-alcoholics[77]. It is estimated that AUD is found in almost 9.75% of patients hospitalized for arrhythmias[78]. The precise mechanism for this increased risk is unclear[79,80]. It has been postulated that both QT interval prolongation and shortening of the atrial effective

refractory period might be related to AF onset after alcohol drinking[80-82]. Long-term abuse is associated with left atrial enlargement and remodeling, which enhances the occurrence of AF[83]. Other mechanisms postulated include diminished vagal and augmented sympathetic heart rate modulation[79,84]. Heavy alcohol intake may also cause ventricular arrhythmias although the risk is much less than that of AF[85]. Data suggest that low to moderate consumption of alcohol confers some protection from serious ventricular arrhythmias[86]. Heavy or chronic alcohol abuse is however associated with an increased incidence of malignant ventricular arrhythmias and higher mortality. Khaliq et al. estimated that the presence of AUD independently increases the risk of mortality by 72% in arrhythmia inpatients[76]. Patients with alcoholic cardiomyopathy also exhibit more ventricular arrhythmias when compared to individuals with idiopathic dilated cardiomyopathy[87]. Mechanisms include cardiomyopathy itself, increased oxidative stress, neurohormonal activation, and altered calcium homeostasis[88,89].

Potassium (K)

Increasing K intake via potassium supplements significantly decreases blood pressure, but the effects of increasing K intake through food alone remain unclear[90]. Reduced serum potassium increases the risk of lethal ventricular arrhythmias in patients with ischemic heart disease, heart failure, and left ventricular hypertrophy[91]. Hypokalemia and hyperkalemia are often seen in hospital settings and are usually treated with therapeutic intervention. Both high and low levels of potassium increase arrhythmias susceptibility[92]. The National Academy of Medicine recommends that adult women have a daily intake of about 2600 mg of K, while adult men have a daily intake of about 3400 mg[93]. Potassium is widely available in many foods, especially fruits and vegetables. Leafy greens, beans, nuts, dairy foods, and starchy vegetables like winter squash, are rich sources[93].

Magnesium (Mg)

Low serum Mg levels have been associated with the development of AF in individuals without cardiovascular disease. A recent Framingham Heart study with 3,530 participants documented that the development of AF was related to a low serum Mg[94]. Magnesium depletion also resulted in AF in several patients if they were limited to about 33% of recommended dietary allowance of Mg intake. Atrial fibrillation has been found in some cases to rapidly resolve with the replacement of Mg[95]. Magnesium administration has been shown to reduce AF in patients undergoing coronary artery bypass surgery[96]. Magnesium is considered a safe and effective treatment in situations of acute AF[97]. Mg also helps against ventricular arrhythmias. In one study, patients with the highest quartile of Mg intake had a reduction of SCD by 77%[98]. IV magnesium has been used in preventing and treating a variety of atrial and ventricular arrhythmias[99]. There are various pathways to Mg insufficiency including reduced intake, reduced absorption, increased loss (GI or renal), excessive sweating, and increased requirements as seen during pregnancy[100]. Alcoholism and several drugs can also reduce Mg levels[100]. However, supplemental Mg and K should be avoided in renal insufficiency. The recommended dietary allowance for Mg for adult men is 400-420 mg per day. The dietary allowance for adult women is 310-320 mg per day[93]. Rich sources of Mg include greens, nuts, seeds, dry beans, whole grains, wheat germ, wheat, and oat bran[93].

Vitamins

Several vitamins with antioxidant, anti-inflammatory, and auto-immune properties have shown benefit in attenuating CVDs (and thereby cardiac arrhythmias)[101]. For example, plasma vitamin C level was inversely associated with the risk of AF in women[102]. One short-term trial showed that supplementation with vitamin antioxidants resulted in a lower probability of AF occurring after on-pump cardiac surgery[103]. However, data on the protective effects of oral supplementation are not persuasive, and oral supplementation is not recommended unless a deficiency is documented. Intake of foods rich in vitamins continues to be a better option.

Fish Oils

A short-term trial showed that a supplement of omega-3 fatty acids was associated with a lower probability of AF occurring after on-pump cardiac surgery[104]. Trials in patients with myocardial infarction also indicate that fish or omega-3 polyunsaturated fatty acids (PUFA) reduce the incidence of fatal CHD[105,106]. The effect seems most pronounced for fatal heart disease and sudden death[64,106-108]. As noted, before, SCD in many cases is preceded by life-threatening ventricular arrhythmias[109]. This supports the hypothesis that omega-3 PUFA from fish oil may help prevent cardiac dangerous arrhythmia. Animal and in vitro studies also indicate that omega-3 PUFA prevents fatal heart disease and SCD by reducing susceptibility for ventricular arrhythmia[110]. As mentioned before, good quality fish oils are a safe way of avoiding environmental contaminants such as mercury that may be present in certain large fish available for human consumption.

Special Diets

Although several individual ingredients (such as fish and nuts) show a beneficial association with AF and SCD, the data presented here applies to the entire dietary pattern. It has been noted in several studies that certain diets result in synergistic effects occurring among their nutritive and nonnutritive components, and their sum effect is often better than that obtained from individual components. Jacobs DR, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: issues and challenges. Am J Clin Nutr. 2003; 78 (suppl): 508S–513S

The Mediterranean diet (MedD) refers to a traditional dietary pattern of people residing around the Mediterranean Sea (Greece, Crete, and Southern Italy) and is regarded as one of the healthiest diets[111]. It is characterized by the consumption of foods abundant in micronutrients, antioxidants, and anti-inflammatory ingredients[112]. Although common in the 1960 and prior years, the diet is being gradually being taken over by the Westernized eating pattern. MedD includes plenty of fruits, vegetables, especially leafy green vegetables, legumes, whole grains, nuts. moderate portions of fish, poultry, and dairy foods like yogurt and cheese. It encourages eating less red meat, meat products, and sweets, and allows wine (in moderation) with meals[113]. Several observational studies have shown that a greater degree of adherence to the MedD decreases the risk of several major non-communicable diseases[114-118] and lowers all-cause mortality[119]. A plethora of studies has also shown that it also provides both primary and secondary protection against CVD morbidity[120,121] and reduces CVD mortality[122]. MedD with

extra virgin olive oil has shown benefits in AF[123,124]. The Prevention with MedD (PREDIMED) trial demonstrated a protective effect on new-onset AF when the MedD was enriched with extra virgin olive oil (EVOO)[125]. In this study of 6,705 participants, the MedD diet with EVOO reduced the risk of AF (hazard ratio=0.62) when compared with the control group[126]. MedD has also shown benefits in SCD. In the Women's Health Initiative, participants in the highest quintile of MedD score experienced a 36% lower risk of SCD, compared with participants in the lowest quintile (after multivariable adjustment)[127]. Likewise, the MedD score was inversely associated with the risk of SCD in the Nurses' Health Study[128]. The REGARDS study (21,069 participants with a mean of 9.8±3.8 years of follow-up). there was a trend toward an inverse association of the MedD score and the risk of SCD after approximately 10 years of follow- up[129].

The Dietary Approaches to Stop Hypertension (DASH) diet is rich in fruits, vegetables, whole grains, nuts, low-fat dairy products, poultry, and fish. There are only small amounts of red meat, sweets, and sugar-containing beverages allowed. Overall, it is low in total and saturated fat, and cholesterol[130,131]. Salt is restricted – the standard version allows up to 2,300 milligrams of sodium per day, and the low-sodium version allows up to 1,500 milligrams of sodium per day. Primarily because of this, DASH helps reduce blood pressure[132,133]. Hypertension (HTN) is a major risk factor for other cardiovascular diseases such as ischemic heart disease, heart failure, and stroke[134]. These CVDs all increase the incidence of AF. In the ARIC (Atherosclerosis Risk in Communities) study, HTN was associated with approximately 20% of incident AF cases. In patients with known AF, HTN is present in about 60% to 80% of those individuals. HTN causes progressive changes in left atrial anatomy and function, which may promote AF through a variety of electrophysiological mechanisms[135,136]. A reduction in systolic blood pressure (≤130 mm Hg) has a 40% lower risk of incident AF compared to those whose systolic blood pressure stays≥142 mm Hg[137,138]. Vermond et al. calculated that the risk of incident AF (HR 1.11) increased with every 10 mm Hg increase in systolic blood pressure[139]. HTN also results in ventricular myocardial scarring, fibrosis, and remodeling and these changes provide a putative basis for ventricular arrhythmogenesis. HTN has been shown to relate to an increased risk of SCD[140]. DASH diet is therefore beneficial in the prevention of both AF and SCD.

Vegetarian Diet

A vegetarian diet is plant-based and does not include any meat intake. Several vegetarian diets have evolved - the lacto-vegetarians eat plant foods plus dairy products, lacto-ovo-vegetarians consume dairy products and eggs, ovo-vegetarians eat eggs, and pesco-vegetarians eat fish and seafood. Vegans completely refrain from all animal-based foods including meat, poultry, eggs, dairy foods, and fish. Vegetarian diets are high in fiber, and typically low in total and saturated fat, intake of n-3 fatty acids, iron, and vitamin B12[141]. They are associated with a reduced risk of major CVDs[142], and this may help reduce the incidence of AF. They also help reduce SCD[143]. Singh et al. found that a vegetarian diet after a myocardial infarction resulted in a significant decrease (34.5%) in total cardiac end points[143]. Complications such as ventricular ectopics (>8/min) and SCD, were significantly decreased in the group eating a vegetarian diet, compared with those eating a control diet.

Low/Very Low Carbohydrate Diets

Low carbohydrate diets increase the risk of incident AF regardless of the type of protein or fat used to replace the carbohydrate. In a large, prospective, cohort study with a long-term follow-up of >20 years, Zhang et al. found that low-carbohydrate intake was associated with a higher risk of incident AF (irrespective of other well-known risk factors for incident AF)[144]. Two potential mechanisms may explain this observed association. First, a low-carbohydrate diet may lead to a lower intake of vegetables, fruits, and grain, and the vitamins they contain, which may reduce anti-inflammatory effects, while stimulating inflammatory pathways[145,146]. Second, a low-carbohydrate diet with increased protein and fat consumption may stimulate oxidative stress[147]. These factors can also increase the risk of other CVDs, which are known risk factors for AF[148]. A diet with a carbohydrate content below <30–50 g/day and fats accounting for 15%–30% of total caloric intake is considered a ketogenic diet by the European Food Safety Authority[149]. Ketogenic diets are contraindicated in several cardiac conditions[150]. They prolong the QT interval, and this may lead to an increase in malignant ventricular arrhythmias and SCD[151].

Conclusion

Cardiac arrhythmias play an important role in cardiovascular morbidity and mortality. Atrial fibrillation is the most common arrhythmia encountered in clinical practice while malignant ventricular arrhythmias are responsible for a significant number of SCDs. There is well-established evidence that a prudent diet plays an important role in beneficially affecting CVDs/ Cardiovascular diseases are a major underlying cause of cardiac arrhythmias. Consumption of certain foods rich in saturated fat, added salt, and excessive alcohol and energy drink consumption appear to be harmful. Intake of coffee, tea, nuts, antioxidant vitamins, and chocolate provide some antiarrhythmic effects. Both the MedD and the DASH diets have shown cardiovascular benefits. In general, plant-based diets, such as the vegetarian diet, are cardio-protective. Clinical studies have provided persuasive data that dietary modification can reduce cardiac arrhythmia incidence and severity. Dietary changes are relatively low-risk and low-cost option to reduce the global cardiac arrhythmia burden.

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