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

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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, 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, or changes in parasympathetic and sympathetic activity[4]. Atrial fibrillation is not benign. It increases the risk of ischemic stroke 5-fold. Globally, stroke is a leading cause of long-term disability and death[5]. AF also increases hospitalization and mortality from ischemic heart disease (IHD) and heart failure[6]. It also increases all-cause mortality[7]. Besides attempts to convert to normal sinus rhythm with drugs like flecainide or to control the heart rate with drugs like beta-blockers and calcium channel blockers, patients with AF also receive oral anticoagulation therapy to prevent future thromboembolic events[8]. Catheter ablation is often used to convert these patients to sinus rhythm[9]. However, relapses 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 underlying cause for SCD is usually a malignant ventricular arrhythmia[13]. It is invariably 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 cause[17]. Most of these individuals die, with the estimated global survival rate of sudden cardiac arrest being 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 (AHA) Strategic Planning Task Force and Statistics Committee suggested monitoring seven simple parameters for better cardiovascular health. These are smoking, body mass index (BMI), physical activity, diet, total cholesterol, blood pressure, and fasting blood glucose[19]. These seven if kept within 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. It is interesting to note that 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 individuals that had no alcohol intake had the lowest loss in health[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 these data, there is ample evidence that following five lifestyles namely, 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 health 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 increased by 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 and Trans-fat/Unsaturated fat

Unprocessed 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 an 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 every 100 kcal/d of red and processed meat is accompanied by a 15-24% lower risk of IHD[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 an increment of one serving per day, 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. These data and data from a plethora of other studies indicate that processed red meat is more dangerous for coronary artery disease (CAD). Jacobsen et al. in a recent overview of systemic reviews confirmed that processed meat intake was associated with a higher risk of CHD and stroke[28]. They specifically increase the risk of myocardial infarction, stroke, and heart failure – all of which are arrhythmogenic[29-31]. The latter occurs due to an autonomic imbalance after an MI and this causes enhanced automaticity in the myocardium and in the conduction system[32,33]. These patients may also have electrolyte imbalances (such as hypokalemia and hypomagnesemia) and hypoxia, which may further contribute to the development of cardiac arrhythmia. Once initiated, the ectopic beat may deteriorate, as the damaged myocardium with changes in its refractoriness,

becomes a substrate for re-entrant circuits.[34-36]. The deleterious link between the consumption of processed and unprocessed red meat and the risk of stroke is also significant. In a study by Kim et al., the pooled relative risks were being 1.11 for red meat intake and 1.17 for processed meat intake[37]. In a large study involving 418,329 men and women from nine European countries (12.7 years of follow-up), Tong et al. reported a higher risk of a stroke with red meat consumption[38]. Besides the known harm a stroke conveys, cardiac arrhythmias, which are highly prevalent during the acute phase of stroke may harm patients by inducing hemodynamic instability and/or resulting in sudden cardiac death[39]. In addition to arrhythmias caused by cardiac comorbidities, several neuro-cardiological interactions further aggravate them in patients with stroke[40,41]. The highest risk for arrhythmia onset is usually in the first 24 hours after admission, during which 74% of all events occurr[42]. Patients after acute stroke also have an increased risk for SCD. In these cases, ventricular fibrillation or pulseless ventricular tachycardia usually underlies leads to cardiac arrest[43,44]. Other arrhythmias seen in these patients are less common and less life-threatening[45]. Cardiac arrhythmias in these patients are also enhanced by associated autonomic dysfunction. There is a loss of overall autonomic modulation, lower parasympathetic tone, impaired baroreflex sensitivity, and a shift toward sympathetic dominance[46].

Heart failure is also more common in patients eating processed 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 (HF) or its related mortality[47]. However, the consumption of processed meat increased the risk of HF - for each 50 g per day increment in intake, the risk of HF increased by 8% (HR=1.08). In this study, the HF mortality increased by 38% (HR=1.38). In women (a cohort of 34,057 Swedish women, 2,806 of whom were diagnosed with HF during 13 years of follow-up), Kaluza et al. reported similar findings. For each 50 g day increase in processed red meat consumption, the risk of HF in this cohort increased by 11%-19%[48]. AF occurs in over half of all patients with HF[49]. Heart failure increases atrial filling pressure and atrial dilatation, leading to atrial scarring and fibrosis.[50]. Atrial tissue stretching is associated with a significant shortening of the atrial refractory period. These factors promote AF[51-53]. Trans fats increase systemic inflammation as well as brain natriuretic peptide levels in HF patients[54]. Fried foods are high in saturated fats and have trans fats. In a large prospective study of 15,362 male physicians, Djoussé et al. found a major increase in HF risk in those with the highest versus the lowest intake of fried food[55].

Dietary patterns that include low-fat dairy are associated with a lower risk of cardiac arrhythmias 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 arrhythmia risk. Most nuts, including peanuts, most tree nuts, and flax seeds are also safe[56]. Ultra-processed food is high in unhealthy fats and its intake is arrhythmogenic[56]. In mice, consumption of a high-fat diet increased the vulnerability to atrial arrhythmia by down-regulation of Cx40 via miR-27b[57]. There is evidence that a high level of trans-18:2 fat in the red blood cell membrane is associated with a markedly higher risk of SCD. Saturated fats and trans-18:2 should therefore be limited in any diet[58]. On the other hand, SCD, which is a leading cause of death in patients with CHD[59-61] is reduced with dietary intake of long-chain n-3 polyunsaturated fatty acids (PUFAs) (such as those

available in seafood)[62]. Even among persons without prior clinical CAD, increased dietary long-chain n-3s PUFAs intake is 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 noted for decades. The benefit of light or moderate alcohol intake on AF is suggested but remains unclear. It has been postulated that a low dose of red wine intake (due to its resveratrol content) may be arrhythmia protective, but clinical trials confirming this relationship are scarce[65]. Excessive alcohol intake is a well-known risk factor for AF, both in an acute or chronic setting. Binge drinking (males = consumption of ≥ 5 standard drinks and females = ≥ 4 standard drinks during one sitting) may lead to the "Holiday Heart Syndrome" – a name given to the frequent occurrence of supraventricular arrhythmias, including AF, in these patients. Reports have also shown that binge drinking may occasionally cause 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, with direct (cytotoxic) and indirect (increased sympathetic and parasympathetic activity) underlying mechanisms. Djousse et al. reported that moderate-to-heavy chronic alcohol consumption (≥3 drinks/d or approximately 36 g alcohol) is associated with an increased AF risk in men[68]. This was also confirmed in men in the Framingham Heart Study[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 also confirmed this association between high levels of alcohol intake and incident AF[66,71-73]. A problematic pattern of alcohol use leads to alcohol use disorder (AUD)[74]. 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% per 1,000 persons-years for cardiac arrhythmias, while heavy drinkers (such as those suffering from AUD) have a higher incidence rate of 20.8% per 1,000 person-years[76.] Studies show that there is an 8% relative risk increase in the incidence of arrhythmia for each drink per day consumed by heavy drinkers when compared to non-alcoholics[77]. Alcohol use disorder is noted in almost 9.75% of patients hospitalized for arrhythmias[78]. The precise mechanism for this increased alcohol-arrhythmia link 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 following alcohol intake[80-82]. Long-term abuse is associated with left atrial enlargement and remodeling, which, as mentioned before, enhances the occurrence of AF[83]. Other mechanisms postulated include diminished vagal and augmented sympathetic tone[79,84]. Data suggest that low to moderate consumption of alcohol confers some protection against serious ventricular arrhythmias[85]. On the other hand, heavy intake may cause ventricular arrhythmias although the risk is much lower than that of AF[86]. 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 (n0n-alcoholic) dilated cardiomyopathy[87]. Mechanisms underlying this increased propensity include cardiomyopathy itself, increased oxidative stress, neurohormonal activation, and altered calcium homeostasis[88,89].

Potassium (K)

Increasing K intake via potassium supplements decreases blood pressure, but the BP-lowering effect from increasing K intake through food alone remains unclear[90]. Hypokalemia and hyperkalemia are often seen in hospitalized patients with IHD, heart failure, and left ventricular hypertrophy[91]. Both high and low levels of K+ increase arrhythmia susceptibility[92]. The National Academy of Medicine recommends that adult women ensure a daily intake of about 2600 mg of K+, while adult men need a daily intake of about 3400 mg[93]. Potassium is available in many foods, especially fruits and vegetables. Leafy greens, beans, nuts, and starchy vegetables like winter squash, are also rich sources[93].

Magnesium (Mg)

Low serum Mg levels have been associated with the development of AF in individuals without CVD. A recent Framingham Heart study with 3,530 participants documented this association. They found that the development of AF was often associated with a low serum Mg[94]. Inadequate intake (33% of recommended dietary allowance) resulting in Mg depletion also caused AF in several patients. Replacement of Mg often resolves atrial fibrillation rapidly[95]. Magnesium administration has been shown to reduce AF in patients undergoing coronary artery bypass surgery[96]. Magnesium is a safe and effective treatment modality in acute AF[97]. Mg level is also associated with ventricular arrhythmias. IV magnesium has been used in preventing and treating a variety of ventricular arrhythmias[99]. In one study, patients with the highest quartile of Mg intake had a reduction of SCD by 77%[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]. The recommended dietary allowance for Mg for adult men is 400-420 mg per day[93]. The dietary allowance for adult women is 310-320 mg per day[93]. Rich sources of Mg include green vegetables, nuts, seeds, dry beans, whole grains, wheat germ, and oat bran[93].

Vitamins

Several vitamins with antioxidant and anti-inflammatory properties are of benefit in CVDs (and thereby cardiac arrhythmias)[101]. For example, in one study, 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 in patients undergoing 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, however, is a better option.

Fish Oils

Omega-3 fatty acids are cardio-protective. A short-term trial found that supplementation with these resulted in a lower probability of AF occurring after on-pump cardiac surgery[104]. Trials in patients with myocardial infarction also indicate that intake of fish or omega-3 polyunsaturated fatty acids (PUFA) reduces the incidence of fatal CHD[105,106]. This benefit is especially noted in patients who are at a higher risk of SCD[64,106-108]. As mentioned above, SCD in many cases is

preceded by life-threatening ventricular arrhythmias[109]. Animal studies also indicate that intake of omega-3 PUFA is associated with a reduction in SCD[110].

Special Diets

It has been noted in several studies that certain combinations of foods result in synergistic effects occurring among their nutritive and nonnutritive components, and their sum effect is often better than that obtained from individual components. The result is better cardiac health.

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 available diets[111]. It is characterized by the consumption of foods abundant in micronutrients, antioxidants, and anti-inflammatory properties[112]. 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 have also shown that it also provides both primary and secondary protection against CVD morbidity[120,121] and CVD mortality[122]. MedD with extra virgin olive oil (EVOO) has shown benefits in the prevention of 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 reduced risk had a 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, when compared with participants in the lowest quintile (after multivariable adjustment)[127]. Likewise, the MedD score was inversely related to the risk of SCD in the Nurses' Health Study[128]. The REGARDS study (21,069 participants with a mean follow-up of 9.8±3.8 years) a trend toward an inverse association of the MedD score and the risk of SCD was noted 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[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 per day. This diet helps reduce blood pressure[132,133]. Hypertension (HTN) is a major risk factor for other cardiovascular diseases such as IHD, heart failure, and stroke[134]. These CVDs all increase the incidence of AF. In the 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%. 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 was≥142 mm Hg[137,138]. Vermond et al. calculated that the risk of incident AF increased (HR=1.11) with every 10 mm Hg increase in systolic blood pressure[139]. HTN also results in

ventricular scarring, fibrosis, and remodeling and these changes encourage ventricular arrhythmogenesis. HTN has been shown to relate to an increased risk of SCD[140]. DASH diet, mainly via its BP reducing property, is therapeutic in the prevention of both AF and SCD.

Vegetarian Diet

A vegetarian diet is plant-based and does not include any meat. 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 also 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, 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]. The latter included ventricular ectopic beats (>8/min) and SCD.

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 carbohydrates. 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]. A low- carbohydrate diet may lead to a lower intake of vegetables, fruits, grain, and the vitamins they contain, thereby stimulating inflammatory pathways[145,146]. Further, a low- carbohydrate diet with increased protein and fat consumption may increase 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 a ketogenic diet according to 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 beneficial role in CVDs. Cardiovascular diseases are often associated with cardiac arrhythmias. Consumption of certain foods rich in saturated fat, and salt appear to be harmful. Excessive intake of alcohol and high consumption of energy drinks is also deleterious to the CVD system. 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 and vegan diet are cardio-protective. Overall 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 options to reduce the global cardiac arrhythmia burden.

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