Impact of Diet on Cardiovascular Diseases: Coronary Artery Disease Risk Factors

Abstract

Coronary artery disease is a leading cause of morbidity and mortality in the world. It is estimated that a large majority of coronary artery disease can be prevented by following healthy lifestyles. Healthy lifestyles are also linked to favorable changes in modifiable risk factors. These include hypertension, diabetes mellitus, dyslipidemia, and obesity. Since atherosclerosis starts in childhood, major lifestyle changes should be initiated at an early age. Modification of the diet is especially important at this age. Data accumulated from several meta-analyses indicate that a plant-based diet rich in fruits and vegetables, whole grains, legumes, nuts, and polyunsaturated fats are heart-healthy. On the other hand, diets rich in red meat, especially processed red meat, saturated fats, sodium, refined carbohydrates, and sugar-sweetened beverages are heart unhealthy. The role of the Mediterranean diet, DASH diet, and the vegetarian diet is also important in reducing the burden of coronary artery disease. This manuscript complements the three-part series on diet and coronary artery disease published earlier.

Keywords: coronary artery disease, obesity, hypertension, dyslipidemia, diabetes mellitus, depression

Introduction

Cardiovascular diseases (CVDs) are the major cause of suffering and death in the world[1]. Coronary artery disease (CAD or coronary heart disease: CHD) is the most common CVD[2]. It has a global prevalence of 2%–3%[3] and is the foremost single cause of loss of Disability Adjusted Life Years (DALYs) and mortality[4,5]. Much of this burden falls on low- and middle-income countries[6]. It is estimated that it affected 110 million people in 2015, was responsible for 164.0 million DALYs, and caused 8.92 million deaths[7]. Although CAD burden decreased in the high-income countries between 1990 and 2017, the rising world population and the increasing number of aged individuals, continue to increase the global crude numbers[8]. Low- and middle-income countries are expected to account for 82% of the future increase in CAD related mortality[9]. According to the World Heart Federation, the global cost of CVD in 2010 was approximately US$863 billion, which is expected to rise to more than US $1 trillion by 2030. In the low and middle-income countries, health expenditure (for CAD) is as high as 10% of the total healthcare expenditure[10].

More than 70% of at-risk individuals have multiple risk factors for IHD, and only 2%-7% of the general population have no risk factors[11]. These are mainly lifestyle factors, and it is postulated that with adequate changes in diet and lifestyle, about 80% of (premature) CVD mortality may be prevented[12]. Diet is one lifestyle that is a major driving force in the pathogenesis of

atherosclerosis[13]. A healthy diet also significantly decreases the risk of CAD by attenuating several modifiable CAD-related risk factors.

Discussion

Nutrition plays an increasing role in the primary and secondary prevention of several diseases, including CVDs[14]. The nutrition cardiovascular connection was first recognized in 1908, when a Russian scientist Alexander Ingatowski, demonstrated that high cholesterol intake caused the development of atherosclerosis in rabbits[15]. Atherosclerosis is the primary cause of coronary artery disease, and this can be attenuated[16] or even reversed with the intake of a healthy diet[17]. A healthy diet should not result in excess body weight (both BMI and WC should be normal) and should also be balanced, providing adequate macronutrients and micronutrients, with a good intake of water. Diets that are primarily plant-based, rich in whole grains, legumes, nuts, and fiber are heart-healthy. They have high amounts of polyunsaturated fats. These diets may include limited amounts of lean red meat and one egg a day. Seafood, low-fat dairy foods are safe. Coffee, tea, and chocolate intake are also beneficial. However, diets rich in red meat, especially processed red meat, saturated fats, trans fats, high levels of sodium and sugar, especially sugar-sweetened beverages and refined carbohydrates are harmful. Several common diets, such as the DASH diet, Mediterranean diet, and the vegetarian diet have CAD preventive effects. A heart-healthy diet also helps reduce several major modifiable risk factors for CAD.

1. Obesity

Obesity is an independent risk factor for CHD[18]. Weight gain increases the risk of CHD events and CHD mortality[19]. A 10 kg rise in body weight increases the risk of CAD by 12%[20]. When the BMI exceeds 30 Kg/m^2, there is a 44% increase in risk for myocardial infarction[21]. Further, obese patients have more complex CHD disease and do not thrive well[22]. Following CABG, obese patients had a higher incidence of deep sternal wound infections[23]. Obese patients with CAD, also have higher mortality and unsatisfactory neurological recovery following a cardiogenic arrest recovery[24]. Adipocytokines from the fatty tissue in overweight/obese individuals induce insulin resistance, endothelial dysfunction, hypercoagulability, and systemic inflammation, promoting the atherosclerotic process[25]. Weight loss in obese CHD patients results in marked improvements in several CHD risk factors such as hypertension, CRP, lipids, insulin resistance, oxidative stress, and thrombogenicity[26]. This results in a lower incidence of CHD events, and reduced CHD mortality[27]. Dietary modification is central to the prevention and treatment of obesity[28,29]. One pound of weight is equal to 3500 Kcal[30]. Increasing calorie intake will therefore increase body weight, if not balanced by increased expenditure. Similarly, reducing caloric intake will induce weight loss. Many weight-loss diets work on this law of thermodynamics[31,32]. Restricting or increasing certain macro-ingredients in the diet also helps reduce weight through several complex mechanisms[33]. Some non-calorie and non-macronutrient restricted diets (such as the Mediterranean and vegetarian/vegan) are associated with a decreased risk of obesity[34,35]. Obesity paradox is an unusual phenomenon, where in an already developed disease, excess weight and obesity are associated with a favorable prognosis. The obesity paradox has also been noted in CAD[36]. Its discussion is beyond the scope of this manuscript.

Hypertension

Hypertension is a major risk factor for CAD[37]. The risk for MI doubles when the systolic pressure is > 140 mm Hg when compared to that between 120 mm Hg and 129 mm Hg[38]. Similarly, compared to a diastolic pressure of <80 mm Hg, the risk ratio for CAD doubles if it increases above 94 mm Hg[39]. Hypertension is common in patients with CAD. In a large analysis of over 122,000 patients from 14 international randomized trials, the prevalence of hypertension in those with established CAD ranged from 30% to 70%[40]. Adverse clinical outcomes are higher in CAD patients if they have co-existing hypertension[41]. Studies have demonstrated that patients requiring more medications for blood pressure (BP) control or those with resistant or uncontrolled HTN have higher rates of adverse CAD outcomes, including all-cause death and nonfatal myocardial infarction[42]. It is estimated that the mortality rate of CHD is 2.3 times greater when hypertension is present[43]. Treatment of HTN results in a decrease in adverse cardiovascular outcomes (both with clinical and subclinical CAD). It is estimated that a modest short-term reduction in blood pressure confers a reduction in CAD events by about 16%[44]. Dietary modifications to reduce hypertension include decreased salt intake, weight loss, and moderation of alcohol consumption (among those who drink). The salutary effects of sodium restriction on BP are well established[45,46]. A meta-analysis (34 trials and 3230 participants) found that a sodium intake reduction of 4.4 g/day decreased BP by 5.4/2.8 mmHg in hypertensive individuals and 2.4/1.0 mmHg in normotensive individuals[47]. Besides its action in reducing HTN, sodium also directly damages target organs via multiple intricate pathways. In contrast to the Western diet, DASH[48], Mediterranean (MedD)[49], vegetarian[50], and Paleolithic[51] diets also help reduce BP. Hypertension exacerbates atherosclerosis by increasing sympathetic drive centrally via activation of the renin-angiotensin-aldosterone system. It increases oxidative stress, inflammatory cytokines, and endothelial and microvascular dysfunction[52]. It also causes a deficiency in vasodilators such as nitric oxide and prostacyclin. Hypertension may also increase afterload and result in left ventricular hypertrophy, which may compromise coronary blood circulation during diastole[53]. Hypertension is also frequently associated with insulin resistance and dyslipidemia, which are additional risk factors of atherosclerosis.

Diabetes Mellitus

CAD is the leading cause of morbidity in diabetic patients[54]. The atherosclerotic process occurs earlier and progresses at a greater rate and extent in the diabetic than in the non-diabetic population. Studies indicate that diabetic patients have more three-vessel disease and a more complicated coronary artery involvement than their nondiabetic counterparts[55,56]. They also have a higher CAD-related mortality[57]. Post-myocardial infarction, diabetic patients have a twofold increase in 30-day and five-year mortality[58,59]. They also have a higher risk for complications post-intervention, including mortality, than nondiabetic subjects[60,61]. Diabetics also have a high prevalence (in 1 in five diabetics) of asymptomatic CAD[62]. Diabetes is now regarded as a CAD risk equivalent[63]. The role of diet in the pathogenesis of T2DM is well known[64]. Maintenance of ideal body weight is important to prevent or control diabetes mellitus[65]. Even a 5 to 7 percent weight loss markedly lowers the risk of progressing to diabetes in prediabetes[66]. Weight loss helps reduce DM by several mechanisms that include reducing ectopic fat[67], reducing glucotoxicity[68,69], and decreasing the demands on beta-cells[70]. The quality of diet is also

extremely important. Indians found that T2DM was almost confined to the rich people who consumed oil, refined flour, and sugar in excessive amounts[71]. Diets that involve ingesting low amounts of saturated fat and refined carbohydrates, including sugar, are associated with a reduced incidence of T2DM[72]. On the other hand, meat-based diets are harmful. In one study, long-term adherence (over a 17-year interval) to a diet that included at least weekly meat intake was associated with a 74% increase (OR = 1.74) in odds of diabetes (compared to those adhering long term to a (no meat) vegetarian diet)[73]. It has been observed that vegetarian diets are inversely associated with the risk of developing T2DM[74]. The Adventist Society reported a 74% reduction in diabetes incidence from a vegetarian diet when compared to a meat-based diet in a 17-year follow-up[75]. Another study put this reduction at 35%[76]. In the Rotterdam study, T2DM risk was reduced by 18% with a vegetarian-based diet after a follow-up of four to seven years[77]. Studies show that lower glycemic index (GI) diets help improve insulin secretion, insulin resistance, body weight, composition, and HbA1c levels[78,79]. GI reflects the glycemic impact of the carbohydrates in a diet (irrespective of quantity) while glycemic load (GL) represents the overall glycemic impact considering both quantity and quality of carbohydrate. Both – high GI and high GL foods are associated with increased incidence of T2DM[80] and CAD[81]. Two common diets used to reduce CVDs, MedD[82] and DASH[83] are also helpful in reducing T2DM. The ATTICA study reported improved fasting glucose and improved insulin levels (15% reduction) with an adherence to the Mediterranean diet[84]. Intake of extra virgin olive oil, a major component of MedD, helps reduce both plasma glucose and HbA1c[85]. It is estimated that MedD reduces HbA1c by 0.32 to 0.53 percentage units[86]. Med D shows these benefits independent of weight loss. Putative mechanisms include improvements in insulin sensitivity via a reduction in inflammation[87] and beneficial effects of fatty acids[88] and phenolic compounds on the beta-cell[89]. The DASH diet, commonly used to decrease sodium intake for the treatment of HTN, also helps against DM. In a systemic review and meta-analysis of five prospective cohort studies (n = 158,408) the consumption of a DASH dietary pattern reduced diabetes incidence by 18% (RR = 0.82)[90]. A vegetarian diet is also helpful[91]. There is, however, little scientific evidence regarding the effects of the Paleolithic diet on T2DM incidence[92].

Dyslipidemia

Lipoproteins are intricately involved in the development and progression of atherosclerosis[93,94]. Increased serum LDL-C is commonly pathogenic in CAD[95]. There is a linear relationship between the plasma concentration of LDL-C and coronary events[96]. The serum LDL-C level should be under 100 mg/dL in high-risk patients, and under 70 mg/dL in very high-risk patients97. There appears to be no threshold below which a further reduction in LDL-C leads to no further atherosclerotic vascular disease prevention[98,99]. Hence LDL-C may be safely lowered as much as possible[100]. Other lipid parameters often associated with an increased risk of CAD include high total cholesterol (TC), high triglycerides (TGs), a decreased level of HDL-C, high TG/HDL-cholesterol ratio, and high TC/HDL-cholesterol ratio[101,102]. Dietary intervention is often used as the initial treatment for dyslipidemia[103-105]. The Western diet is high in saturated fatty acids (SAFA). Replacing SAFA with unsaturated fatty acids in the diet (especially with polyunsaturated fatty acids (PUFA), lowers LDL-C without affecting HDL-C and TGs[106-108]. Replacing SAFA with carbohydrates does not improve the overall blood lipid profile. It lowers LDL-C but also lowers HDL-C and raises fasting TGs[109]. Supplemental intake of omega 3 PUFAs (EPA and DHA), from fish oil, helps lower TG concentrations[110]. Another component of

the diet that significantly affects the lipid profile is soluble fiber (SF). It has been calculated that an intake of 4–10 g/day of SF results in a 5–10% reduction in LDL-C without substantially affecting HDL-C and TG concentrations[111]. Reducing SAFA and increasing SF intake can also be achieved by following several special diets. The MED dietary pattern significantly lowers LDL-C by −0.07 mmol/L and TGs by −0.46 mmol/L[112] - this beneficial change was however not seen in another recent study[113]. MedD adherence also improves HDL-C levels[114]. The DASH diet is also good for dyslipidemia. Siervo et al. however, in a meta-analysis of 1917 participants observed a reduction in TC (-0.20 mmol/L) and LDL-C levels after the DASH intervention (−0.10 mmol/L) while there were no significant differences in HDL-c and triglyceride levels[115]. Similar results were obtained in a recently published controlled trial in 80 T2DM patients after 12 weeks following the DASH diet[116]. A 2019 umbrella review of systematic reviews and meta-analyses concluded that the DASH diet lowered the TC by −0.20 mmol/L and LDL-C by −0.10 mmol/L - without affecting HDL-C and TGs[117]. Two meta-analyses of randomized controlled trials (RCTs) found that vegetarian diets significantly lowered TC by −0.32 to −0.36 mmol/L and LDL-C by −0.32 to −0.34 mmol/L[118,119]. Vegetarian diets in these studies however also lowered HDL-C by −0.09 to −0.10 mmol/L while TGs were not significantly altered. A recent meta-analysis of RCTs in T2DM patients found that vegetarian diet patterns led to a reduction in LDL-C of −0.12 mmol/L with no significant effects on HDL-C and TGs[120]. In a recent meta-analysis of 36 RCTs, the substitution of red meat with plant-based protein foods showed a reduction in total cholesterol and LDL-C levels[121]. Ketogenic diets also appear to reduce TG levels (-0.18 mmol/L and increase HDL-C levels (+0.09 mmol/L)[122].

Sleep disturbances

Abnormal sleep duration or disturbed sleep increases the risk of CAD. A sleep duration of ≤6 hours/night or ≥10 hours/night of sleep results in a higher prevalence of CHD, when compared to a reference group sleeping 7 to 9 hours[123]. In another study, the risk of CHD, at the end of a 10-year follow-up was 1.39-fold higher in women reporting <5 hours/night and 1.37-fold higher in those sleeping >9 hours compared to those sleeping 8 hours/night[124]. Similar data were reported in the Women's Health Initiative Study. In this study, compared to 7–8 hours of sleep per night, self-reported sleep of <5 hours or >10 hours, was associated with a 25% and a 43% respectively, raised risk for CHD[125]. Abnormal sleep duration also affects mortality. Cappuccio and group reported that fatal CHD was greater in those with a habitual sleep duration above or below 7 to 8 hours[126]. Several dietary components may affect sleep[127]. Tryptophan consumption improves sleep[128]. This amino acid is present in milk[129]. Conversely, the depletion of tryptophan has been shown to reduce sleep quality[130]. Tryptophan crosses the blood-brain barrier, where it is converted to serotonin, the precursor to the sleep-promoting hormone, melatonin[131]. Melatonin and serotonin intake in foods such as cherries is also associated with improvements in sleep duration and quality[132]. Sleep may also be disturbed by abnormal respiration, such as seen in obstructive sleep apnea (OSA)[133]. In a meta-analysis, it was noted that OSA resulted in an increased risk of incident clinically overt CAD in adults, especially in men[134,135]. Sleep apnea is estimated to confer a two-to threefold increase in poor cardiovascular outcomes and in all-cause mortality[136]. A Spanish study of 1,500 patients (10 year follow-up) demonstrated a reduction in coronary artery disease with CPAP treatment in these patients[137]. Obesity plays an important role

in OSA, with the incidence of OSA in people with obesity being as high as 30%[138]. Weight loss in these patients, either by dietary intervention or by bariatric surgery leads to a reduction in apnea-hypopnea index (AHI)[139,140]. In one study, the benefits in AHI persisted over 4-years despite patients regaining 50% of the lost weight by the 4th year[141]. The mechanisms behind OSA leading to a higher incidence of CAD may be related to the intermittent hypoxia causing sympathetic nervous system overactivity and increased inflammation, oxidative stress, and endoplasmic reticulum stress[142].

Smoking and Physical Inactivity

Smoking and inadequate physical activity are both connected with unhealthy diets. Smokers eat poorly. Alkerwi et al found an inverse relationship between the intensity of tobacco consumption and overall diet quality[143]. Smokers also tend to have less physical activity, drink more, and are less adherent to special diets[144,145]. People with healthier diets and less obesity are more likely to be more active[146]. The reverse is also relevant as more active people are less likely to be obese.

Chronic Kidney Disease

Chronic Kidney disease (CKD) patients have a five to tenfold higher risk for developing CAD[147]. Besides the traditional risk factors such as hypertension, diabetes mellitus, obesity, etc. CKD patients are also exposed to many nontraditional, uremia-related risk factors, such as an abnormal calcium-phosphorus metabolism[148]. There is an abrupt decline in CAD risk after kidney transplant, despite years of exposure to traditional CAD risk factors[149]. In early CKD stages, the adoption of a healthy diet (primarily plant-based - a high intake of vegetables, fruits, nuts, whole grains, legumes, fish, fiber, and polyunsaturated fatty acids but low in saturated fatty acids and sodium.) slows glomerular filtration rate (GFR) decline and progression to end-stage renal disease (ESRD)[150,151]. Mortality is also reduced[152,153]. Salt restriction in CKD patients is beneficial irrespective of its antihypertensive effects[154]. Western diets include a substantial amount of meat and salt. Consumption of two or more servings per week of red meat was associated with more microalbuminuria and a faster decline in estimated GFR[155,156]. The consumption of two or more high-sugar content beverages has been reported to increase the risk of glomerular filtration impairment and proteinuria[157]. High consumption of sugary drinks/sodas leads to a faster decline in the GFR[158]. Fructose is especially harmful in CKD[159]. Brymora et al. demonstrated diminished inflammatory parameters, as well as lower fasting serum insulin levels and BP in patients with stage 2 and 3 CKD after they were switched to a low-fructose diet for 6 weeks[160]. A low protein diet offers a variety of clinical benefits in patients with renal insufficiency. A high protein diet may increase kidney damage[161]. Therefore, regular counseling with a nutritionist is required in these patients to ensure adequate protein and energy intake and to avoid or correct protein-energy-related wasting.

Depression:

Several studies have shown a depression CAD link. In one meta-analysis of several prospective studies of individuals initially free of CHD, depression increased the risk of incident CHD by 30%[162]. The presence of depression in CHD patients also prognosticates poor outcomes, including a higher incidence of chest pain and shortness of breath, higher re-hospitalization rates,

and a greater risk of non-fatal cardiovascular events[163,164]. Depression significantly affects functionality after an MI and worsens the QOL[165]. Patients with CHD and associated depression also have significantly increased mortality after an angiographically confirmed diagnosis[166-168], following an acute coronary syndrome[169] and following coronary artery bypass graft surgery[170]. Analyses of many trials indicate that prognosis improves in these patients when depression improves. Several observational and clinical studies have shown that diet plays an important role in the pathogenesis of depressive disorders. Plant-based diets, rich in olive oil, whole grain, fish, low-fat dairy, and low in animal foods lead to a decreased risk of depression[171,172]. A Western diet, rich in red and/or processed meat, saturated fats, refined grains, sweets, high-fat dairy products, and low in fruits and vegetables is associated with an increased risk of depression[173,174]. Obesity, often a consequence of poor diet, also increases the risk of depression[175]. On the other hand, individuals with depression are also more likely to consume poorer quality diets[176] and more likely to become obesity[177].

Psychological Stress

Prospective studies show that chronic stress or long-term repetitive stress exposure (such as job stress, marital unhappiness, caregiving burden, or feeling of being treated unfairly)[178] is associated with a 40–50% increase in CAD[179,180]. Acute mental stress (for instance, anger, emotional turbulence) is more common and results in more cardiovascular events and more severe events, compared to chronic stress[181-183]. Stress impacts diet negatively. Stress decreases diet quality and contributes to consuming unhealthy foods such as fast foods, sweets, and other fat and energy-dense foods. The increased consumption of these hyper-palatable foods that are low nutrient-dense (e.g., butter, cream cheese, full-fat products), occurs in stressed individuals even when there is no hunger or bodily demand for food[184,185]. Further, stress lowers the intake of fruits, vegetables, fish, and unsaturated oils[186]. Poor diet quality is detrimental to the coronary vascular system. Stress can also affect the amount of food intake. Stress often results in over-eating[187] and binge-eating[188]. This leads to obesity, which as discussed above, is harmful to CAD[189].

Conclusion

Diet has direct effects on the coronary vasculature. However, there are several major modifiable risk factors for CAD that are also affected. These include obesity, hypertension, diabetes mellitus, dyslipidemias, improper sleep, chronic kidney disease, and mood disorders. Even smoking and low physical activity relate to diet. Many of these relationships are bidirectional. Overall, a plant-based diet with small amounts of lean meat, the absence of trans fats, and low in sodium and added sugars is helpful. MedD, DASH, and vegetarian/vegan diets are also useful in combating these risk factors.

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