Impact of Diet on Cardiovascular Diseases: Coronary Artery Disease

Part II: Unhealthy Macronutrients, Special Diets, and Obesity

"Dis-moi ce que tu manges, je te dirai ce que tu es."

[Tell me what you eat, and I will tell you what you are].

Anthelme Brillat-Savarin, 1826

Author:

Shashi K. Agarwal, MD

2227 US Highway 1, Suite 309, North Brunswick, NJ 08902, USA

Abstract

The role of red meat especially processed red meat, and its deleterious relationship with coronary artery disease is well known. A multitude of studies have demonstrated that processed red meat, saturated fats, refined carbohydrates, and sugar- sweetened beverages increase the risk of coronary artery disease. Trans fats and ultra-processed foods are extremely harmful. Trans fats must be completed avoided and ultra-processed food intake must be markedly reduced or also completely avoided. A replacement of saturated fats by mono-unsaturated fats and poly-unsaturated fats reduces coronary heart disease risk. Diet is also intricately connected with obesity and a BMI >30 results in an increased coronary artery disease morbidity and mortality. Central or abdominal obesity is even more harmful. The Western diet is rich in unhealthy foods. Unfortunately, a Western style of eating is gradually replacing healthier diets all over the world. The role of Mediterranean, DASH, and vegetarian diets in reducing the pathogenesis of coronary artery disease are also discussed.

Key words: coronary artery disease, red meat, saturated fats, obesity, Mediterranean diet, DASH, vegetarian diet

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death in almost every region of the world[1,2.] According to the World Health Organization (WHO) 2015 statistics, CVDs account for > 17.7 million or 31% of all deaths worldwide[3]. The major culprit is coronary heart disease

(CHD). Besides imparting enormous human suffering, coronary artery disease (CAD) inflicts huge direct and indirect financial costs on worldwide society[4]. With the ready availability of affordable therapeutics globally, and the relative slowdown in the introduction of newer modalities, lifestyle interventions are gaining importance to further control this epidemic[5]. An unhealthy diet is consistently blamed for higher risk of CHD incidence and mortality[6]. Therefore, modulating the diet, from unhealthy to healthy, is an important goal in the quest for further improving global CHD health. This paper is a narrative review of the effect of unhealthy diet on CHD. Several common diets are also reviewed. Part I of this 3-part manuscript discussed the role of several healthy food choices. This part deals with unhealthy macronutrients, obesity, and some special diets. The role of micronutrients in the pathogenesis of coronary heart disease is discussed in part 3 of this 3-part manuscript.

The diet eaten in the Western countries is rich in red meat, both processed and unprocessed, saturated fats, ultra-processed foods, refined carbohydrates, and sugar-sweetened beverages[7]. This diet not only affects the coronary arteries, but also results in obesity. Obesity, especially visceral or abdominal obesity, is a major contributor to coronary atherosclerosis[8]. This eating pattern is responsible for most cases of CAD[9]. This manuscript will discuss harmful macronutrients associated with such a diet. Some beneficial diets include the Mediterranean diet, Dash diet, and vegetarian diet. The beneficial effects of these diets are also discussed.

Red Meat: Unprocessed and Processed

Meat is eaten all over the world[10]. Red meat encompasses beef, veal, pork, lamb, venison, horse meat, and mutton. Total red meat consumption is associated with a higher CHD risk. An increased risk of CHD of 19%, was noted in the Nurses' Health Study (84,136 women), per serving of unprocessed red meat/day[11]. A prospective study of 409,885 men and women in nine European countries showed a similar increase in the risk of CHD for every 100 g/day increment 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[12]. 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[13]. 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[14]. Associations have also been noted with red meat ingestion and CHD mortality. A meta-analysis of 13 cohort studies (1,674,272 individuals) found that those with the highest intake had an 18% (processed red meat) and 16% (unprocessed red meat) higher risk of CVD mortality[15]. Al-Shaar, et al. noted that for CHD mortality, the HR was 1.38 total red meat, 1.29 for unprocessed red meat, and 1.21 for processed red meat[13]. This study also did a multivariate adjustment for dietary and non-dietary risk factors. Replacing red meat consumption with healthier choices protects the vascular system. Veno et al. found lower rates of large artery atherosclerosis when processed red meat (HR: 0.78)

or unprocessed red meat (HR: 0.87) was replaced with fish[16]. Lean red meat may be neutral or even beneficial[17,18].

Red meat is high in saturated fat. Red and processed meats also provide heme-iron - higher levels contribute to oxidative stress through the promotion of low-density lipoprotein (LDL-C) oxidation[19]. Furthermore, advanced glycation end products formed during the cooking of red meat increase inflammation and likely contribute to the observed effect on CVD[20]. Finally, red meat provides L-carnitine and phosphatidylcholine that are metabolized to trimethylamine N-oxide (TMAO), a compound associated with increased risk of CVD and adverse cardiac events[21]. Processed red meat (such as hot dogs, ham, sausages, frankfurters, salami, and bacon) undergoes curing, smoking, salting, or the addition of chemical preservatives (such as sodium – 400% more than unprocessed meat and nitrites) to extend its shelf life[22]. It also has additives added to improve flavor, color, and quality – which may be harmful to the cardiovascular system.

Fats

Saturated fats are solid[23]. They exert harmful effects on CVDs[24-27]. A high HR of 1.26 for >5 g/day intake of meat was seen for CVD in the Multi-Ethnic Study of Atherosclerosis Study. An even higher HR of 1.48 was noted if >5% energy came from saturated fats from meat[28]. In an evaluation of data from 59,000 participants, Cochrane analysis reported that reducing saturated fat intake reduces the CVD event rate.[29]. There was a 17% increase in the risk of CHD with each increase of 5 percent of energy intake from saturated fat, as compared with equivalent energy intake from carbohydrates in the Nurse's Health Study[30]. In a systemic review and meta-analysis, Chowdhury et al. also showed that dietary fat intake was associated with an increased risk of CHD[31]. The American College of Cardiology (ACC)/American Heart Association (AHA) recommend that foods high in saturated fats (e.g., meat, full-fat dairy products, and tropical oils such as coconut and palm oil) should be limited to achieve <7% of energy from saturated fatty acids (SFA)[32]. Replacing saturated fats with monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs) is also helpful and their use is inversely associated with CHD[33,34]. In a nearly 30-year study involving 84, 628 women and 42, 908 men, it was noted that there was a 25% and 15% reduction in CHD risk if 5% of calories from SFAs were replaced with the equivalent energy from PUFAs, MUFAs, respectively[35]. A meta-analysis of four trials also showed a significant reduction (relative risk= 0.71) in CHD with a replacement of SFAs with MUFAs and, PUFAs[36]. A decrease in CHD also occurs if total saturated fat is replaced by an isocaloric intake of omega 3 fatty acids, a plant-based diet, or whole grains. However, an isocaloric replacement of SFA with trans fats, omega 6 fatty acids, processed animal fat, refined carbohydrates, starches, and high fructose corn syrup increased the risk of CHD[37-43]. In the 2020–25 Dietary Guidelines Advisory Committee report, the ACC/AHA recommends replacing foods high in saturated fats with foods high in unsaturated fats, especially MUFA and PUFA for CVD prevention and reducing CVD mortality[44].

MUFA

Replacing hydrogenated fats with MUFA results in improvements in several CVD risk factors. These include total cholesterol (TC), LDL-L, high density lipoprotein cholesterol (HDL-C), triglycerides (TG), apoprotein A-1, and lipoprotein (a)[45]. Mensink et al. found that MUFA rich

diet resulted in higher HDL-C levels, with a reduction in TG levels and the ratio of TC to HDL-C[46]. In a subsequent meta-analysis, it was observed that high MUFA intake was associated with a significant improvement in LDL-C, Apo A-1, and Apo B[47]. In a recent meta-analysis, it was noted that high MUFA diets in overweight/obese individuals also significantly reduced systolic and diastolic blood pressure[48]. The most frequently consumed MUFA rich dietary oils are canola and olive oil. Other common sources are peanut oil, avocados, unsalted nuts: almonds, peanuts, pecans, pistachios, hazelnuts, English walnuts, edamame, hemp seeds, chia seeds, flax seeds, and fenugreek seeds.

PUFA

Polyunsaturated fatty acids (PUFAs) are fats that tend to be liquid at room temperature. PUFAs can be omega-3 or omega-6. Fish is rich in omega-3 and plant oils are rich in omega-6. Replacing saturated fat with linoleic acid, an essential polyunsaturated omega-6 fatty acid, reduced the cholesterol by about 10% in 17 intervention trials, and reduced major coronary events by 13%[49]. In the Nurses' Health Study, (78,778 US women with 20 years of follow-up) PUFA intake was associated with a decreased CHD risk (multivariate relative risk or RR of 0.75) for the highest vs. the lowest quintile[50]. In an extensive systematic review of 15 trials with 10,076 participants, Abdelhamid et al. found that high intake of PUFA reduced CHD events from 14.2% to 12.3% (RR= 0.87)[51]. In the same study, high PUFA intake was also associated with a slight reduction (from 6.6% to 6.1% with an RR 0.91) in the risk of CHD death[51]. PUFAs are present in soybean, corn, and sunflower oil, and some nuts and seeds, tofu, and soybeans. PUFA affect hepatic LDL receptor activity resulting in lower LDL-C levels.

Trans Fats

Solid fats usually contain higher proportions of saturated fats, whereas liquid oils are richer in mono- and polyunsaturated fats[52]. Trans fats (TFA) are produced by partial hydrogenation of saturated fats. They help lengthen products' shelf lives and reduce costs. TFAs, originally considered a healthy substitute for SFAs[53] were subsequently found to increase LDL-C and decrease HDL-C, causing an increased risk of CVDs and CVD related mortality[54,55]. In the Framingham study of 832 men ages 45-64 years and free of CHD, a significant increase in the risk of CHD was noted with the intake of margarine – a major source of TFAs[56]. After a 20-year follow-up in the Nurses' Health Study, Oh et al. also reported that the intake of trans fats was related with an increased risk of CHD (RR=1.33), especially in younger women[50]. The WHO guidelines limit TFA intake to 1% of energy intake and have indicated its desire to the elimination of TFA from the global food supply[57]. The recent ACC/AHA guidelines recommend that there should be no intake of trans fats to reduce atherosclerotic CVD risk[58]. Trans fats may be present in pastries, cakes, donuts, cookies, fried foods such as French fries, fried chicken, onion rings and deep-fried snacks cooked in re-used oil, stick margarine, shortening, butter, meat, cheese, and dairy products.

Fried Food

The INTERHEART study (5761 cases and10,646 controls from 52 countries) found a 13% higher risk of CAD (Odds Ratio=1.13) when the highest to the lowest tertile of fried foods consumption was compared[59]. There have been several studies showing an association between

fried food consumption and several major CAD risk factors such as being overweight[60]. Type 2 diabetes mellitus (T2DM)[61], hypertension (HTN)[62], and decreased HDL-C[63].

Ultra-processed foods

Ultra-processed foods are increasing worldwide[64]. It is estimated that in many countries, they account for 25% and 60% of total daily energy intake[65]. Ultra-processed foods have a higher content of total fat, saturated fat, added sugar, energy density, and salt, along with lower fiber, vitamins, and minerals. They also contain additives, colorings, flavorings, sweeteners, and emulsifiers, many of them harmful to health[66]. However, they are tasty, cheap, and convenient. In a study with 105,159 participants (21,912 men and 83,247 women) with a median follow-up of 5.2 years, intake of ultra-processed food was associated with a higher risk of CHD (hazard ratio 1.13)[67]. Their ingestion is also associated with weight gain[68]. They are also associated with an increase in abdominal obesity (OR: 1.62)[69]. Most ultra-processed foods are commonly available as snack food such as chips, cheese puffs, candy bars, snack cakes, and cookies or fast food such as French fries, chicken nuggets, shakes, soda, etc. It is estimated by a Centers for Disease Control and Prevention (USA) study that during the years 2013 to 2016, nearly 40 percent of Americans ate fast food on any given day.

Refined Carbohydrates

Refined carbohydrates may be milled grain, starches, or sugar. Milling the grain removes the bran and germ and this improves shelf life. However, processing increases the caloric density by > 10%, reduces the amount of dietary fiber by 80%, and reduces the amount of dietary protein by almost 30%[70]. This leaves a starchy carbohydrate with fewer nutrients[71]. Examples are bread and tortillas containing white flour, bagels. Waffles, pastries, instant noodles, breakfast cereals, white rice, and pizza. The intake of refined carbohydrates is on the rise in low- to middle-income countries[72,73], especially those in Asia[74]. There was an approximate 50% increase in the intake of refined carbohydrates in the Alaskan Inland Inuit from 1955 to 1957 to 1965. This has been causally connected to the subsequent increase in atherosclerosis and CAD in this population[75]. The detrimental effect of an increased intake of refined carbohydrates has been noted in several studies. The Nurses' Health Study and the Health Professionals Follow-up Study also showed that intake of carbohydrates from refined starches and added sugars were positively associated with an increased risk of CHD (HR: 1.10), when extreme quintiles were compared[35].

Sugar/Sugar Sweetened drinks

Sugar is a refined carbohydrate. Sugars are classified into monosaccharides (glucose, fructose, and galactose) and disaccharides (maltose, sucrose, and lactose). The monosaccharide, fructose, and fructose-containing disaccharides (e.g., sucrose) produce greater degrees of metabolic abnormalities than does glucose. They may present a greater risk of CHD. WHO recommends that <10% of total energy intake should come from free sugars[76]. Free sugars include monosaccharides and disaccharides added to foods and beverages, sugars in sugar-sweetened drinks, and sugars naturally present in honey, syrups, fruit juices, and fruit juice concentrates. People who derive 10–25% of their caloric intake from sugar have a 30% higher risk for cardiovascular mortality[77]. Those deriving more than 25% calories from sugar, which is roughly

on par with average sugar consumption in the US and Germany, the relative risk of cardiovascular mortality is nearly tripled[77]. A significant contribution of added sugar comes from the consumption of processed food like bakery products and sweet snacks[78]. In industrially produced food, sugar is often used to enhance flavor and attenuate suppression of appetite[79]. It is estimated that nearly 50% of added sugars are ingested through sugar-sweetened beverages (SSBs) such as soda, tea, and fruit drinks[78]. SSBs are high in sucrose (containing 50% saccharose and 50% fructose) and high fructose corn syrup (containing up to 55% fructose). Sugar-sweetened beverage consumption has been positively associated with CHD[80,81]. This has been confirmed by a meta-analysis of cohort studies[82]. African American participants who consumed high fructose corn syrup (HFCS) sweetened soda almost every day (5–6 times/week) had two times the CHD risk, and participants who consumed any combination of HFCS sweetened soda and fruit drinks ≥3 times/day had more than 2.5–3 times the CHD risk, compared to seldom/ never consumers[83].

Several mechanisms are involved in this increased risk of CAD. Intake of SSBs is associated with risk of hypertension[84], obesity[85], and diabetes[86]. Each additional sugar-sweetened drink consumed daily raises the risk of developing diabetes by approximately 25%[85,87]. It also increases the blood levels of TG, TC, and LDL-C[88].

Even diet drinks are not safe. In a population-based cohort study of 39,786 participants over 18 years, daily diet soft drink consumption increased the risk of IHD[89]. The National Health Service and Health Professionals Follow-Up Study showed both sugar-sweetened and low-calorie sodas significantly increased the risk of CHD by 20%[90]. Sugar substitutes increase the risk for obesity, weight gain, metabolic syndrome, T2DM, and CHD. The sugar substitutes interfere with glucose and energy homeostasis, destroy the healthy microbiome, alter leptin levels, and decrease satiety[91].

Energy Drinks

Most energy drinks are caffeinated. Intake of up to 200 mg as energy drinks appear to be safe in young healthy adults[92]. However, higher intakes may cause severe adverse cardiac effects in some participants, such as palpitations and prolonged QT interval[93].

Diet and Obesity

Diet also plays an important role in causing excess body weight. Excess weight is defined as: Overweight: body mass index (BMI) 24.9–29.9 kg/m^2. Class 1 obesity 30–34.9 kg/m^2, Class II obesity 35–39.9 kg/m^2, and Class III obesity >40 kg/m$^{2.}$ Abdominal obesity/central/visceral obesity is diagnosed if the waist circumference >35 inches in men and >32 inches in women[94] or a waist/hip ratio above 0.9 in men and above 0.85 in women[95]. Overweight and obesity are independent risk factors for CHD[96]. In young individuals, obesity is related to an increased incidence of both non-ST segment elevation myocardial infarction (NSTEMI)[97] and ST-elevation myocardial infarction (STEMI)[98]. Overall, it is estimated that a 10 kg rise in body weight increases the risk of CAD by 12%[99]. Obese patients have more complex CHD disease and have more complications[100]. Adipocytokines from fatty tissue induce insulin resistance, endothelial dysfunction, hypercoagulability, and systemic inflammation, and these promote the

atherosclerotic process. Dietary modification is therefore central to the prevention and treatment of obesity[101]. Weight loss in obese CHD patients results in marked improvements in several CHD risk factors such as hypertension, C-reactive protein (CRP), lipids, insulin resistance, oxidative stress, and thrombogenicity[102]. This results in a lower incidence of CHD events, and reduced CHD mortality[103]. The impact of an elevated blood pressure (BP) on CAD is significant: a 2-mmHg increase in BP increases mortality from CAD by 7 percent[104]. Weight loss also improves the lipid profile. A weight loss of 5–8 kg, induces a mean LDL-C reduction of 5 mg/dL and an increase in HDL-C by 2–3 mg/dL. A 3 kg weight loss reduces TG by 15 mg/dL[105]. Scientific data indicates that each 1% reduction in LDL-C or non-HDL-C is associated with a 1% decrease in CHD event risk over 5 years[106]. Inflammation plays a major role in atherosclerosis and weight loss is associated with a significant decrease in CRP levels[107]. Many other CHD beneficial changes also occur, such as a decrease in blood glucose and an increase in insulin sensitivity[108], a reduction in oxidative stress[109], and decreased thrombogenicity[110].

The National Heart, Lung, and Blood Institute of America recommends that daily calorie intakes in the United States (US) be around 2,500 for men and 2,000 for women[111]. One pound of weight is equal to 3500 Kcal and increasing caloric consumption will increase body weight, if not balanced by increased expenditure[112]. Similarly, reducing caloric intake will induce weight loss. Many weight-loss diets work on this law of thermodynamics. Restricting or increasing certain macro-ingredients in the diet also helps reduce weight through several complex mechanisms[113-116]. Some non-calorie and non-macronutrient restricted diets are also associated with decreased risk of obesity. Diets such as Mediterranean[117] and vegetarian/vegan[118] can also help prevent weight gain and reduce obesity.

Western Diet

The western diet is a typical example of unhealthy food intake. The Western diet is higher in the intake of red meat, refined grains, processed meat, French fries, sweets and dessert, high-fat dairy products, and sugar-sweetened drinks[119]. It is low in green leafy vegetables and fruits. Studies showed that the consumption of a Western diet significantly increases the LDL-C, TC, fasting TG, BP, BMI, and waist circumferance[120-123]. This increases CAD[124]. The Western diet is increasingly being adopted by low to middle income countries and this has been associated with an increasing incidence of CAD[125,126].

Mediterranean Diet (MedD)

The MedD is defined as a traditional eating pattern found among populations living in the Mediterranean Basin[127]. This diet includes very low consumption of red meat (beef, pork, and lamb are reserved only for special occasions), very low or no consumption of processed meats, occasional intake of poultry, low or no consumption of butter, ice cream, or other whole-fat dairy products (only fermented dairy products, cheese, and yogurt, are consumed in moderate amounts)[128]. It includes an abundant consumption of olive oil, especially extra-virgin olive oil[129], together with high consumption of minimally processed, locally grown, fresh vegetables, fresh fruits, nuts, legumes, and cereals (mainly unrefined). An important source of protein is a moderate consumption of fish and shellfish. The diet also includes a moderate consumption of wine[130]. There is a good calorie distribution in this diet. MedD has significant cardio-protective

effects. A meta-analysis of several cohort studies showed that adherence to MedD reduced cardiovascular events by 10% and mortality by 8%[131]. In the PREDIMED study, MedD provided significant primary protection against myocardial infarction MI) by about 30%[132]. The EPIC-NL trial also reported a reduction in the occurrence of MI (HR-0.86)[133], In the Spanish section of the EPIC study, there was a 40% reduction in the risk of CAD occurrence in the patients highly adherent to MedD (hazard ratio: 0.60 after adjusting for confounders)[134,135]. The Lyon Diet Heart Study provided evidence that MedD was also effective for secondary prevention. In this study, MedD was able to reduce MI plus cardiovascular death by 72%, MI plus cardiovascular death plus major secondary events (unstable angina occurrence, overt heart failure, stroke, or pulmonary or peripheral embolism) by 67% and these plus minor events requiring hospital admission, including recurrent stable angina, postangioplasty restenosis, surgical or medical myocardial revascularization, and thrombophlebitis by 47%[136]. A sub-analysis of the GISSI-Prevenzione study involving patients surviving recent (3 months or less) MI, there was a 14% reduction in the overall risk of mortality after 6.5- year follow-up[137]. A prospective analysis from Iestra et al. in patients following MedD with a recent MI, showed a significant reduction in mortality risk (hazard ratio: 0.75)[138]. In a study of 74,886 women 38 to 63 years of age in the Nurses' Health Study, and without a history of cardiovascular disease and diabetes, during a 20 years of follow-up, were divided into a top quintile amd a bottom quintile. The former group experienced a lower risk of CHD (RR=7.1)[139]. The MedDiet is high in unsaturated fatty acids (MUFA and PUFA), polyphenols, flavonoids, phytosterols and fiber, which protect atherosclerotic plaques from progression and instability, leading to a reduced risk of CVD. A marked reduction in inflammation (reduced IL-6 and IL-8, monocyte chemotactic protein-1, TNF-a, adhesion molecules) is a major mechanism for cardiovascular risk prevention[140]. The MedD diet also helps in reducing weight and improving glycemic control in T2DM[141,142] – both are risk factors for CAD. Extra virgin olive oil and red wine play an important role in the beneficial effects of MedD[143-146]. Widmer et al. indicated the benefits of MedD were comparable to those seen with customary non-invasive therapeutics (aspirin, statins, antihypertensives) in reducing the risk of cardiovascular disease morbidity, mortality, and other deletrious events[147].

The Dietary Approaches to Stop Hypertension (DASH) diet

DASH diet is rich in fruits, vegetables, whole grains, legumes, and nuts. It also includes low-fat dairy. seafood, skinless poultry, moderate intake of alcohol (for adults). It is low in red and processed meats, saturated fats, refined grains, sodium, and sugar-sweetened foods and beverages[148,149]. DASH diet is protective for CHD. In the Nurses' Health Study, with 88,517 female nurses aged 34 to 59 years without a history of cardiovascular disease or diabetes enrolled in 1980, during a 24 year follow up, there was an inverse relationship between DASH diet and incident nonfatal MI[150]. In a meta-analysis of cohort studies, there was a 21% reduced risk of CAD in DASH followers[151]. A similar inverse association was noted in a longitudinal study of 153,082 US veterans (HR 0.82)[152]. In the Singapore Chinese Health Study, involving 57,078 participants aged 45 to 74 years, a greater adherence to the DASH dietary pattern was significantly associated with a lower risk of CAD (HR= 0.76)[153]. DASH diet reduces CAD primarily by its effect on lowering BP[154,155]. The reduction noted is both in hypertensives (systolic BP: −11 mm Hg) and in normotensives (3 mm Hg)[156]. DASH diet has a favorable effect

on the lipids[157]. It also decreases inflammation[158]. DASH diet also lowers the risk of T2DM - a meta-analysis of 4 prospective studies showed a 22% lower risk of T2DM when comparing the highest to the lowest DASH score categories[159].

Vegetarian diet

Vegetarian diets are of various kinds. A vegan diet does not contain any animal products (meat, fish, poultry, eggs, or dairy) and consists of plant-based foods, such as fruits, vegetables, whole grains, and legumes/beans. Pesco-vegetarian (pescatarians) diet avoids meat or poultry but does allow fish and shellfish, eggs, and dairy, in addition to plant-based foods, such as fruits, vegetables, whole grains, and legumes/beans. Semi-vegetarians or "flexitarians"– eat all foods, including meat, poultry, fish and shellfish, eggs, and dairy, in addition to plant-based foods, such as fruits, vegetables, whole grains, and legumes/beans – they however limit their red meat and poultry intake[160].

In the European Prospective Investigation into Cancer and Nutrition Oxford study, which included 48,188 participants and had a 18 years of follow-up, the incidence of CAD was significantly lower among vegetarians and pescatarians when compared with meat-eaters[161]. Vegetarian dietary patterns reduce CVD mortality and the risk of CHD by 40%[162]. Vegetarian diets also reduce CHD mortality. A meta-analysis of 5 prospective dietary studies evaluated long-term CAD mortality rates among vegetarian and nonvegetarian cohorts from Western countries. Compared with regular meat-eaters, CAD mortality was 34% lower in pescatarians, 34% lower in lacto-ovo-vegetarians, 26% lower in vegans, and 20% lower in occasional meat-eaters[163].

Vegetarian diets are rich in fiber, carbohydrate, potassium, magnesium, folate, n-6 fatty acids, non-heme iron, and vitamin C when compared with non-vegetarian diets[164]. Studies have shown that vegetarians and vegans, compared to omnivores, have a lower BMI, and lower levels of LDL-C, glucose, hsCRP, and trimethylamine-N-oxide (commonly known as TMAO) levels[165-171]. Individuals on vegetarian diets lower their BP, lose weight, and improve glycemic control to greater extent than omnivorous comparison diets[172-174]. The vegetarian patterns of eating may however decrease the intake of certain nutrients - such as vitamins B12 and D[175]. Supplementation, consumption of fortified foods, and in the case of vitamin D, sunlight exposure can help ensure adequate levels.

Conclusion

A significant number of people in this world are omnivores. Non-fried poultry eating appears neutral in its effects, while consumption of processed red meat is extremely harmful to the coronary arteries. Processed red meat is high in sodium, saturated fats, nitrites, and several additives. Saturated fats are also conducive to atherosclerosis and should be replaced by unsaturated fatty acids. Trans fats are especially harmful and should be completely avoided. Ultra-processed food consumption is also harmful, and their consumption should be reduced as much as possible. Sugar and sugar-sweetened beverages are also associated with a higher incidence of CAD. Besides its quality, the amount of caloric intake in the diet is also important. Obesity has consistently been causally associated with CHD. A diet such as the Mediterranean,

DASH, and vegetarian are primarily plant-based and have consistently been shown to improve CHD morbidity and mortality. Part III of this manuscript reviews the micronutrients and supplements that impact CHD.

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