Associations between food diets and atherosclerosis risk: a comparative analysis study

Abstract

Background and Objective: Diet is an important, protective, and/or aggravating factor of atherosclerosis; this disease is the main factor of cardiovascular events representing the most common cause of death worldwide. The purpose of this study was to perform a systematic analysis comparing and assessing the effect of several diets on atherosclerosis risk.

Methods: The database, PubMed, was the subject of a search of articles published in English. The selected studies were related to published epidemiological and observational or cohort trials discussing the effects of different diets on atherosclerosis, as well as articles examining risk factors sharing the ability to accelerate atherosclerosis development.

Results: 60 studies were included with an independent and comparative analysis of six different diets. The results of these studies suggest, on the one hand, the significant effect of the Mediterranean diet, which has been supported by many studies explained by numerous advantages. The DASH « *Dietary Approach to Stop Hypertension* » diet has positive effects primarily on blood pressure, which is one of atherosclerosis risk factors. Additionally, the Vegetarian Diet, the Portfolio Diet, and the Okinawa Diet show established benefits in preventing coronary heart disease. However, the Western diet reveals cardiovascular and metabolic harmfulness with an increased risk of carotid atherosclerosis.

Conclusion: Throughout this systematic review, it is evident that the Mediterranean diet is the main protector of atherosclerosis. This finding has been shown by several scientific studies suggesting its benefits against cardiovascular disease.

Keywords: Diet, Atherosclerosis, Cardiovascular events, Systematic review**.**

1. Introduction

Diet has constantly been a crucial component for human health. Convincing evidence supports that eating habits positively or negatively influence dyslipidemia and decreased or worsened the risk of cardiovascular diseases (CVD) (Schwingshackl et al. 2017; Estruch et al. 2018). Nutritional strategies aimed at delaying or preventing chronic disease, especially cardiovascular disease, which is the leading cause of death worldwide, are of utmost interest (Badimon et al. 2019).

Atherosclerosis is the dominant cause of CVD. Atherosclerosis is commonly considered to be a contemporary era disease, it has been present in humans for over 5,000 years, and is associated with advanced modern lifestyles and diets (Frostegård, 2013; Minelli and Montinari, 2019). Cardiovascular diseases, and primarily atherosclerosis, could be prevented by adopting a healthy diet based on fruits, vegetables, low-fat dairy products and lean red meat, on one hand, and on limiting the consumption of soda and sodium chloride, on the other hand. Moreover, sufficient intakes of vitamins, minerals and polyunsaturated fatty acids such as Omega-3 and Omega-6 are highly recommended (Sharifi-Rad, 2020).

Dietary lifestyles are organized around a pivotal notion generally known as diets. Several diets exist, and are generally related to the geographical locations and/or the targeted therapeutic approach (Sharifi-Rad, 2020). Firstly, the Mediterranean diet is the best known and most recommended and scientifically studied, then, the Okinawa, the western diet, the « *Dietary Approach to Stop Hypertension* » DASH and other kind of diets are currently being studied and a growing interest in them is observed in recent years for their therapeutic purpose in association with several types of diseases and complications (Jimenez-Torres, 2021).

In this article, we summarize, through a systematic comparative analysis, evidences linking atherosclerosis risk to different diets and dietary approaches, namely; Mediterranean diet, western diet, DASH approach, vegetarian diet, portfolio diet, and the Okinawa diet.

2. Materials and methods

2.1 Research methodology

The search was performed on PubMed electronic database. several combinations of search terms are used containing one or more of the keywords: ("Mediterranean diet" OR "Okinawa diet" OR "Okinawa vegetables" OR "dietary pattern in Japan" OR "Western dietary pattern" OR "Western diet" OR "Western populations" OR "DASH diet" OR "Dietary Approaches to Stop Hypertension" OR "vegetarian diet" OR "plant-based diet" OR "Vegan diet" OR "Portfolio diet" OR "dietary Portfolio") AND ("atherosclerosis" OR "endothelial function" OR "lipoprotein oxidation" OR "anti-inflammatory" OR "hyperlipidemia" OR "cholesterol" OR "Weight" OR "Blood pressure").

2.2 Studies Selection

Studies were selected for several raisons. Exclusion criteria comprise experimental studies (on animals), documents other than scientific articles, articles published before 2002 (i.e. over 20 years), articles written in a language other than English, and articles not subject to research (according to the keywords).

Inclusion criteria are based on observational or cohort epidemiological studies published on the relationship between different regimens studied and atherosclerosis. As well as, articles examining risk factors that promotes the atherosclerosis development.

Titles and abstracts of the articles were then examined, in order to allow the eligible studies identification.

Figure 1, shows a flowchart (flow diagram), which describes and clarifies the process and the different steps leading to the selection of studies included in our systematic review, according to the PRISMA model (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes).

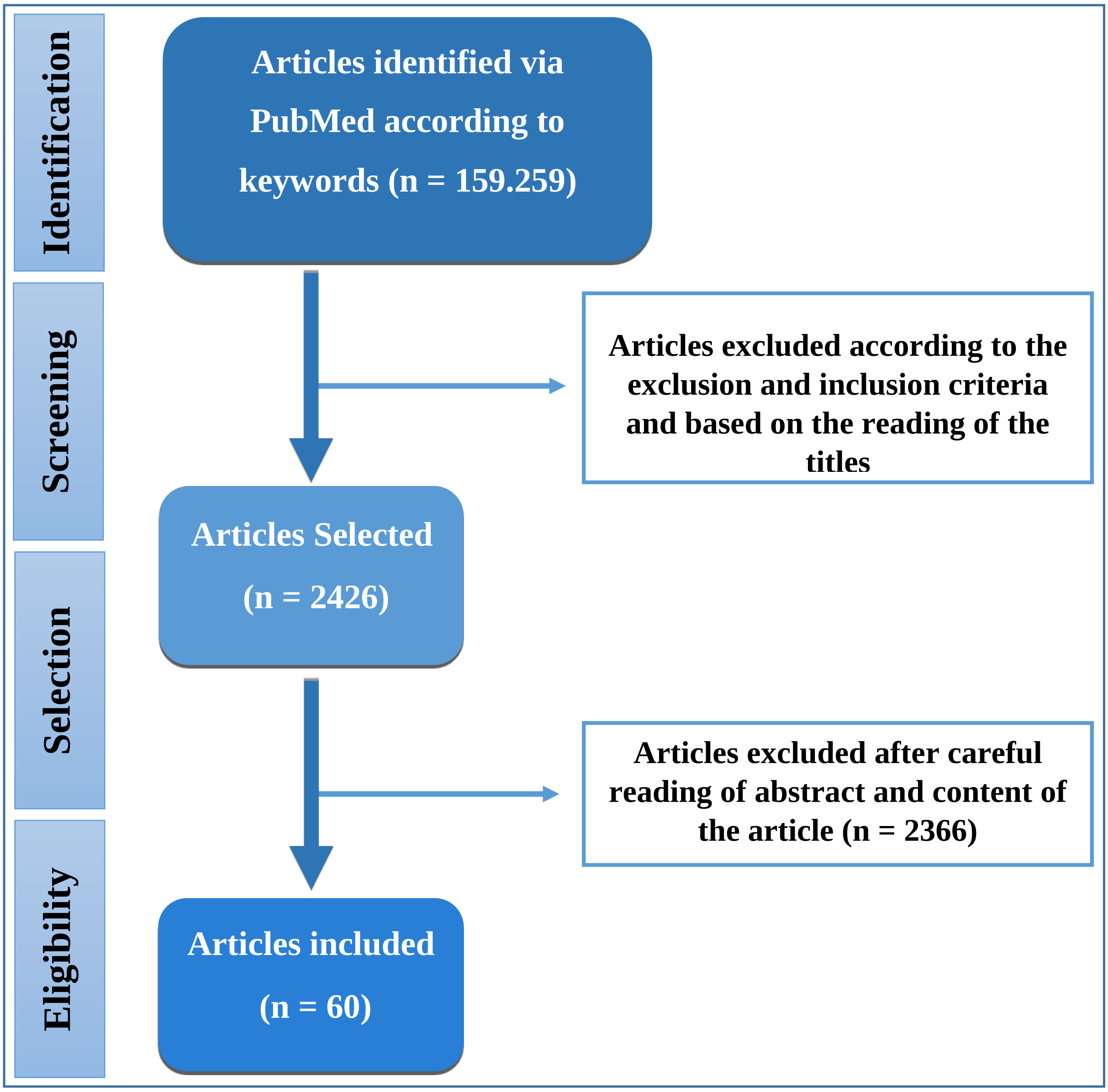

Figure 1. Flow chart of study selection process

3. Results and Discussion

The employed keywords on the database made it possible to reference 159,259 publications. After analysing by title and according to the exclusion and inclusion criteria, 2426 articles appeared. Then, basing on abstracts and the articles content, 60 studies were identified, retained and were therefore included in the systematic review for being independently reviewed. The data extraction from each study is based on the authors' names, the publication year, methodology and the main outcomes cited.

Diet has different effects on various risk factors for atherosclerosis, ranging from lipid profile to body weight and blood pressure through atheroprotective mechanisms.

Our analysis shows, in a first study, that the Mediterranean diet (MD) could be beneficial in lowering the frequency of metabolic syndrome as well as being related with a significant decrease in inflammatory indicators and in insulin resistance (Esposito et al. 2004), therefore, may be useful for the prevention of type 2 diabetes (T2D) (Khalili-Moghadam et al. 2019) (table 1). In the cross-sectional study performed by Issa et al. (2011) a decrease in body mass index (BMI) (0.510 kgm^{-2} in men and 0.784 kgm^{-2}in women) as well as a decrease in waist circumference (2.77 cm in men and 4.76 cm in women) are observed with the Mediterranean food model. Moreover, lipid profile was also improved, with a decrease in (low density lipoproteins) LDL cholesterol and triglyceride levels (Sofi et al. 2018); it would also make it possible to decrease body weight (Barnard et al. 2021). Likewise, a reduction in the obesity risk (Shatwan et al. 2021) was confirmed over 3 years (Mendez et al. 2006) under the MD diet.

In the randomized controlled trial of Toledo et al (2013), conducted in patients at high cardiovascular risk, a beneficial effect of the MD supplemented with virgin olive oil or nuts on blood pressure has been suggested. This effect is also maintained after six months of adherence to this diet, resulting in reduced systolic blood pressure and improved endothelial function (Davis et al. 2017).

The MD diet allows a significant reduction in the levels lipids and oxidized LDL (Fitó et al. 2007), it is also associated with a decrease in endothelial dysfunctions (Marin et al. 2011). In another study, Mena et al, reported a regulation of inflammation biomarkers linked to atherogenesis such as the expression of adhesion molecules, pro-inflammatory CD_{40}, interleukin-6 (IL-6) and the level of C-reactive protein was decreased (Mena et al. 2009).

The MD can affect the burden of atherosclerotic carotid plaque (Gardener et al. 2014), decreases the vulnerability of the plaque by decreasing the factors of instability (IL-18) and increased the stability factors (IL-10, IL-13) (Casas et al. 2017). Although this diet is high in virgin olive oil, an amelioration in the atheroprotective functions of HDL and a deterioration in the LDL atherogenicity have been observed (Hernáez (a) et al. 2017; Hernáez (b) et al. 2017).

Similar to the MD, the Okinawa diet exhibits beneficial changes in plasma lipids (table 2), decreased levels of total and LDL cholesterol, thus exhibiting reduced carotid artery intima-media thickness (Tatsukawa et al. 2004). Although, this diet was not significantly associated with the risk of T2D, neither in men, nor in women (Nanri at al. 2013), due to the higher vegetable consumption in Okinawa diet (Yamamoto et al. 2020). The Okinawa diet acts on the risk of cardiovascular mortality (Okuda et al. 2015) and prevents coronary heart disease (Yoshizaki et al. 2020). However, the preventive role of metabolic syndrome disappeared with the addition of red meat (Damião et al. 2006). Other foods characterise the Okinawa diet, including high consumption of fish, and have 18% to 19% lower risk of cardiovascular mortality (Yamagishi et al. 2008).

The Western diet has negative effects that contribute to a higher risk of T2D (table 3), especially in men at high genetic risk (Qi et al. 2009). Additionally, the Western diet includes higher animal protein consumption that is commonly related to an elevated risk of T2D (Malik et al. 2016). In the study of Welsh et al. (2010) added sugar consumption (caloric sweeteners used as ingredients in processed or prepared foods) significantly decreased (high density lipoproteins) HDL cholesterol, but increase (triglycerides) TG and LDL. The impacts of this diet, include coronary artery disease progression (Oikonomou et al. 2018) associated with a higher risk of carotid atherosclerosis through increased intima-media thickness of the carotid artery (Wang et al. 2020).

The DASH diet would provide some beneficial effects on blood pressure, total cholesterol, and LDL (Chiu et al. 2016); it also allows an increase in HDL cholesterol levels (table 4). The DASH diet has an important role in the control of cardiometabolic risks even in diabetic patients (Azadbakht et al. 2011). There is an improvement in CVDs risk factors under this diet (Said et al. 2021). The DASH diet has a preventive effect against T2D (Liese et al. 2009), as well as the risk of obesity (Farhadnejad et al. 2018) and could be effective for other pathologies, in particular metabolic syndrome (Ghorabi et al. 2019). Hikmat & Appel (2014) studied the DASH diet efficacy in lowering blood pressure in patients with or without metabolic syndrome. In another study, Juraschek et al (2017) reported that the DASH diet lowered systolic blood pressure, these results are consistent with those of Cohen et al, suggesting that a nutritional model of DASH type may be associated with lower systolic blood pressure in young people (Cohen et al. 2017). This diet induces a decrease in the concentration of C-reactive protein and reduces the plasma concentration of the chemokine CXCL4 in patients with coronary atherosclerosis (Makarewicz-Wujec et al. 2020).

The vegetarian diet is known for its protective effect demonstrated by a decrease in LDL in men, but at lower HDL levels in men and women (Jian et al. 2015), these results are seen in both genders alike (Huang et al. 2014). Kim et al (2012) found lower cholesterol and body fat levels but lower oxidative stress levels in vegetarians (table 5). The protective effect of the lacto-ovo-vegetarian diet is also found regarding the metabolic syndrome. These findings were linked to low values of total cholesterol, LDL, but also a lower HDL (Chiang et al. 2013).

The vegetarian diet can be protective against systolic and diastolic blood pressure with a decrease in the incidence of hypertension (Chuang et al. 2016). The study of Ho et al (2017) indicates a systolic blood pressure of 119.0 mm Hg and 125.1 mm Hg for diastolic blood pressure, which are revealed in ovo-vegetarian women and which were lower than those of vegans and consumers of meat. In the same study, it appeared lower systolic blood pressure (71.11 mmHg) than non-vegetarian males (77.50 mmHg), however, higher systolic blood pressure (105.44 mmHg) was observed than non-vegetarian women (99.84 mmHg), although LDL concentration levels are higher than non-vegetarians (Saintila et al. 2020). Yang et al. (2011) have investigated the impact of vegetarian diets on cardiovascular risk factors, such as lower blood pressure and a lower BMI; a reduction in LDL, total cholesterol and HDL was associated with a reduction in the carotid intima-media thickness, as well as, lower concentrations of total cholesterol, LDL, apo B / apoA I ratio suggest that the vegetarian diet may have a beneficial effect on cardiovascular protection (Kuchta et al. 2016). This vegetarian diet have an anti-inflammatory effect on patients with coronary artery disease, by decreasing the C-reactive protein (Shah et al. 2018), this preventive effect of coronary artery disease is compatible with another study based on a lacto-ovo-vegetarian diet allowing modulation of lipid profiles (Djekic et al. 2020).

The Portfolio diet is often advocated for cholesterol-lowering purposes and would result in 29% reductions in LDL as well as reductions in the LDL / HDL ratio, apolipoprotein (apo) B / apo A, and TC / HDL ratio (Jenkins et al. 2002; Jenkins et al. 2006) (table 6). These reductions result in significant decrease in the risk of coronary heart disease over 10 years (Jenkins et al.

2011). The benefits of this diet have been recognized by the 4 basic components combined including plant sterols, soy protein, viscous fiber, and almond (Jenkins et al. 2003), which are no different in the potency of Statins, to achieve lipid objectives (Jenkins et al. 2005), each of these 4 components, plant sterols have contributed to a very significant reduction in LDL (Jenkins et al. 2008). In another study, the Portfolio diet was proven to be beneficial in lowering blood pressure, with a reduction in cardiovascular disease (Jenkins et al. 2015). Additionally, other authors show the same lipid profile improvements, that are consistently maintained following a Portfolio diet which was directly associated with reductions in total cholesterol (from 207 mg / dL to 142 mg / dL) and LDL cholesterol (from 135 mg / dL to 76 mg / dL) (Richard et al. 2019). The Portfolio diet provides an additional result induced by a decrease in LDL of about 13% (Ramprasath et al. 2014) resulting in reduced concentrations of fat-soluble vitamins (Ramprasath et al. 2014). Note that a Portfolio diet has an impact on the smallest subclasses of LDL (diameter < 25,5 nm) (Gigleux et al. 2007).

4. Conclusion

Based on the studied diets, the Mediterranean diet, which is the richest in components such as olive oil, discloses countless advantages as the improvements in the endothelium regenerative capacity, the regulation of the inflammation related atherogenesis biomarkers and beneficial effects on reducing LDL atherogenic particles. On the other hand, the DASH diet shows positive side in reducing blood pressure, as one of atherosclerosis risk factors, as well as inreducing plasma concentration of the chemokine CXCL4. The vegetarian diet can be protective against coronary artery disease with its anti-inflammatory activities. Likewise, the Portfolio Diet could significantly reduce LDL cholesterol and affects the smallest subclasses of LDL, which are most atherogenic. The Okinawa diet is another protective diet that has benefits in preventing coronary heart disease, associated with a lower risk of cardiovascular mortality. However, the Western diet has cardiovascular and metabolic impacts on coronary heart disease progression and risk of carotid atherosclerosis increase.

Studies that raise the relationship between diet and the risk of atherosclerosis are still under scrutiny, and conclusions are sometimes drawn on the basis of subtleties that seem neglected in other studies.

5. References

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Table 1 Characteristics of included studies evaluating the Mediterranean Diet effect

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Esposito et al.	2004	180	NR	2 years	Metabolic syndrome	MD	↓ IL-6, IL-7, IL-18 and CRP. ↓ Body weight ↓ BMI. ↓ Insulin resistance.
Mendez et al.	2006	27827	29-69	3 years	Obesity Overweight	MD	↓ Incidence of obesity after adherence to MD and was not associated with overweight in ♀ (OR1 0.99, 0.78-1.25) or in ♂ (OR1 1.11, 0.81-1.52).
Fitó et al.	2007	372	55-80	3 month	High cardiovascular Risk	Low-fat diet 2 TMD (TMD + virgin olive oil or TMD + nuts).	↓ ox LDL in the 2 TMD. ↓ SBP (*p*=0.008), DBP (*p*=0.03) in the 2 TMD. ↓ CT, HDL and LDL/HDL cholesterol ratios in the TMD, more than in Low fat diet. ↓ TG ↑ HDL, in the TMD + nuts
Mena et al.	2009	106	55-80	4 years	T2D CVDs risk	Low-fat diet 2 TMD (TMD+virgin olive oil or TMD+nuts).	↓ sVCAM-1 ↓ CRP ↓ CD40 in the TMD+virgin olive oil. ↓ sICAM-1 and IL-6 in the 2 MD.
Marin et al.	2011	20	>65	4 weeks	good health	MD saturated fatty acid diet; a low-fat, high-carbohydrate diet	↓ EMPs ↑ EPCs, after the MD than after the other 2 diets.

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Issa et al.	2011	798	40-60	June-August	Adiposity	MD	↓ BMI of 0.510 kgm^{-2} in ♂ and 0.784 kgm^{-2} in ♀. ↓ WC of 2.77 cm in ♂ and 4.76 cm in ♀.
Toledo et al.	2013	7 158	55-80	4 years	High cardiovascular risk	Low-fat diet 2 TMD (TMD + virgin olive oil or TMD + nuts).	↓ BP in the 2 MD and a low-fat diet ↓ DBP important in the 2 MD -1.53 mmHg (95% CI -2.01 to -1.04) for MD+virgin olive oil and -0.65 (95% CI -1.15 to -0.15) for MD+nuts .
Gardener et al.	2014	1374	66±9	3 years	carotid atherosclerosis	MD	↓of burden of carotid atherosclerotic plaque, after greater adherence to a MD.
Casas et al.	2017	66	55-80	3 and 5 years	High cardiovascular risk	Low-fat diet 2 TMD (TMD + virgin olive oil or TMD + nuts).	↓ Inflammatory Chemokines (20% MCP-1,15% MIP-1 β) ↓ Inflammatory Cytokines (30-50% for IL-5, TNF- α, IFN- γ. 35-40% for IL-6, IL-8) in both MD. ↓ Instability factors (IL-18) and ↑ Stability factors (IL-10, IL-13). ↓ sVCAM-1 in TMD+nuts.

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Davis et al.	2017	166	>64	6 month	good health	MD or habitual diet	↓ SBP (*p*=0.02), NS for DBP (*p*= 0.14). ↑ Percentage of FMD 1.3%.
Hernáez et al.	2017	296	NR	1 Year	High cardiovascular risk	Low-fat diet 2 TMD (TMD + virgin olive oil or TMD + nuts).	↑ Capacity to directly counteract LDL oxidation after the TMD + virgin olive oil. ↑ HDL vasodilator capacity (promote the production of NO) after the TMD + virgin olive oil.
Hernáez et al.	2017	210	NR	1 Year	High cardiovascular risk	Low-fat diet 2 TMD (TMD + virgin olive oil or TMD + nuts).	↑ LDL resistance against oxidation after the 2 TMD. ↑ LDL particle size after the TMD+virgin olive oil. ↓ Remnant cholesterol ↓ TG after TMD+nuts. ↓ Cytotoxicity of LDL particles after the TMD+virgin olive oil. NS after TMD+nuts.
Sofi et al.	2018	118	18-75	3 month	Cardiovascular risk Body weight	MD Vegetarian diet	↓ Body weight (-1.77 kg) in MD, (-1.88 kg) in VD. ↓ BMI (-0.67 kg/m) in MD, (-0.64 kg/m) in VD. ↓ LDL (–5.44%) in VD. ↓ TG (–5.91%) ↓ IL-17 in MD.

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Khalili-Moghadam et al.	2019	2139	20-70	2006-2008 to 2012-2014	T2D risk	MD	Adherence to the MD was associated with lower risk of T2D (HR = 0.48; 95% CI 0.27−0.83).
Barnard et al.	2020	62	NR	36 weeks	Overweight adults	MD or Low-Fat Vegan Diet	↓ Body weight (6.0 kg) in Low-Fat Vegan Diet. ↓ SBP, ↓ DBP (6.0 and 3.2 mmHg, respectively) in MD
Shatwan et al.	2021	961	20-55	NR	Obesity	MD	↓ HC (*p*=0.04) and inverse association between the adherence to MD and BMI (*p*=0.0003). ↓ Risk of obesity.

NR, not reported; **IL**, interleukin; **CRP**, C-reactive protein; **BMI,** body mass index; **MD**, Mediterranean diet; ♀, women ; ♂, man; **OR**, odds ratio; **TMD**, traditional Mediterranean diet; **LDL**, Low Density Lipoproteins; **SBP**, systolic blood pressure; **DBP**, diastolic blood pressure; **TC**, total cholesterol; **HDL**, High Density Lipoproteins; **TG**, triglycerides; **T2D**, type 2 diabetes; **CVD**, cardiovascular disease; **sVCAM-1**, soluble Vascular Cell Adhesion Molecule-1; **sICAM-1**, soluble Intercellular Adhesion Molecule-1; **EPC**, endothelial progenitor cell; **WC**, waist circumference; **BP**, blood pressure; **CI**, confidence interval; **MCP-1**, monocyte chemotactic protein-1; **MIP-1β**, macrophage inflammatory protein-1β; **TNF-α**, tumor necrosis factor-α; **IFN-γ**, interferon-γ-inducing factor; **FMD**, flow-meditated dilation; **NO**, nitric oxide; **NS**, not significant; **VD**, vegetarian diet; **HR**, hazard ratio; **HC**, hip circumference; ↑ ,Increase ; ↓ ,Decrease

Table 2 Characteristics of included studies evaluating the Okinawa diet effect

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Tatsukawa et al.	2004	1078/ 2353	20-89	1999-2000	CRF of carotid atherosclerosis	Okinawa diet	↓ TC, LDL and ↓ IMT. ↑ BMI.
Damião et al.	2006	151	40-79	7 years	MS	Japanese eating habits	Usual consumption of red meat was positively associated with MS especially among ♂.
Yamagishi et al.	2008	57972	40-79	12 years	CVDs	High fish consumption	↓ Risk of CVDs mortality from 18% to 19%.
Nanri et al.	2013	64705	45-74	5-10 years	T2D	Dietary patterns of Japanese and Western population	↑ Risk of T2D for the westernized model. No association with the risk of T2D for the Japanese.
Okuda et al.	2015	9112	30-79	24 years	CVDs	High consumption of fruits and vegetables	↓ Risk of CVDs mortality in Japan (HR were 0.74).
Yamamoto et al.	2020	10732	45-74	5 years	T2D	High vegetable consumption	Okinawan vegetables consumed were not associated with the risk of T2D in ♂ and ♀.
Yoshizaki et al.	2020	16498	45-74	5 years	Coronary heart disease	High vegetable consumption	Okinawan vegetables were not significantly associated with the risk of CVDs such as coronary heart disease.

CRF, cardiovascular risk factors; **TC**, total cholesterol; **LDL**, Low Density Lipoproteins; **IMT**, intima-media thickness; **BMI**, body Mass Index; **MS**, Metabolic syndrome; ♂, men; ♀, women; **CVDs**, cardiovascular diseases; **T2D**, type 2 diabetes; **HR**, hazard ratio; ↑, Increase ; ↓, Decrease.

Table 3 Characteristics of included studies evaluating the Western diet effect

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Qi et al.	2009	2533	40-75	1986-2000	T2D	Western diet	↑ Risk of T2D in ♂ with high GRS.
Welsh, et al.	2010	6113	>18	1999-2006	Dyslipidemia	Western diet	↓ HDL ↑ TG ↑ LDL
Malik et al.	2016	15580	30-55 ♀ 40-75 ♂	18-24 years	T2D	Western diet	↑ Animal protein intake associated with 7% risk of T2D.
Oikonomou et al.	2018	188	NR	NR	Coronary heart disease	Western diet	Significant impact in the progression of coronary artery disease.
Wang et al.	2020	1246	42-52	1996-1997 2001-2003 2005-2007	Carotid atherosclerosis	Western diet	Significant association with a higher CCA-IMT.

T2D, type 2 diabetes; ♂, men; ♀, women; **GRS**, genetic risk score**; HDL**, High Density Lipoproteins; **TG**, triglycerides; **LDL**, Low Density Lipoproteins; **NR**, not reported; **CCA-IMT**, carotid artery intima-media thickness; ↑, Increase; ↓, Decrease.

Table 4 Characteristics of included studies evaluating the DASH diet effect

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Liese et al.	2009	862	40-69	5 years	T2D	DASH diet	Inverse association with incidence of T2D
Azadbakht et al.	2011	31	NR	8 weeks	Cardiometabolic risks	DASH diet	↓ LDL (-17.2 ± 3.5 mg/dl; *p*=0.02). ↑ HDL (4.3 ± 0.9 mg/dl; *p*=0.02). ↓ SBP (-3.1± 2.7 mm Hg; *p*=0.02) ↓ DBP (-0.7±3.3 mm Hg; *p*=0.04). ↓ Body weight (*p*=0.007).
Hikmat & Appel.	2014	99/311	22	11 weeks	Blood pressure	DASH diet	↓ SBP 4.9 mm Hg, DBP by 1.9 mm Hg in subjects with MS. ↓ SBP 5.2 mm Hg, DBP by 2.9 mm Hg in subjects without MS.
Chiu et al.	2016	36	21	6 weeks	Dyslipidemia	DASH diet	↓ BP ↓ TC ↓ LDL
Cohen et al.	2017	9 793	8-18	2003-2012	Weight and blood pressure	DASH diet	Inverse association between DASH diet and SBP among 14-18 year olds and 11-13 year olds. No relation to weight status.
Juraschek et al.	2017	412	≥ 22	4 weeks	Blood Pressure	DASH diet	Progressively greater ↓ of SBP.

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Farhadnejad et al.	2018	628	10-18	3 years	CRF of CVDs	DASH diet	↓ Risk of general obesity (OR = 0.26, 95% CI: 0.15 to 0.76) and central obesity (OR = 0.32, 95% CI: 0.14 to 0.84). No significant association with risk of dyslipidemia.
Ghorabi et al.	2019	396	≥18	April 2017 - March 2018	MS	DASH diet	A significant inverse association with the odds of MS (OR: 0.28, 95% IC : 0.14-0.54) ; for elevated BP (OR: 0.12, CI 95%: 0.05-0.29), and reduced levels of HDL (OR: 0.32, 95% CI: 0.18-0.57).
Makarewicz-Wujec et al.	2020	96	>18	6 month	Coronary atherosclerotic lesions	DASH diet	↓ CRP (-0.085 ± 0.15 ng/ml) ↓ CXCL4 (-3.35 ± 3.4 ng/ml)
Said et al.	2021	92	≥ 40	12 weeks	CRF of CVDs	DASH diet	↓ BMI by 6,5% ↓ SBP by 6.9% ↓ TC by 5,2% ↓LDL by 8.2% ↑ HDL by 8.2%

T2D, type diabetes**; DASH**, *Dietary Approaches to Stopping Hypertension*; **CRF**, cardiometabolic risk factor; **LDL**, Low Density Lipoproteins; **HDL**, High Density Lipoproteins; **SBP**, systolic blood pressure; **DBP**, diastolic blood pressure; **MS**, metabolic syndrome; **BP**, blood pressure; **TC**, total cholesterol; **CVD**, cardiovascular disease; **OR**, odds ratio; **CI**, confidence interval; **CRP**, C-reactive protein; **BMI**, body mass index; ↑ , Increase ; ↓ , Decrease.

Table 5 Summary of characteristics of included studies that evaluate the effect of the vegetarian diet

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Yang et al.	2011	171	21-76	1 year	CRF of CVDs	Vegetarian diet	↓ BMI ↓ SBP ↓ DBP ↓ TG ↓ TC ↓ HDL ↓ LDL ↓ Apo A ↓ Apo B ↓ cIMT (*p*<0.05)
Kim et al.	2012	75	40-65	2010-2011	Low oxidative stress, body fat, and cholesterol levels	Vegetarian diet	↓ Body fat of 21.6% ↓ Levels of ROM (*p*<0.011) ↓ TC ↓ LDL
Chiang et al.	2013	706	50-70	May 2007 - April 2008	MS	Ovo-lacto-vegetarian diet	↓ Risk of MS ↓ TC ↓LDL ↓HDL ↓ TC / HDL Ratio
Huang et al.	2014	3551	≧15	1 year	Blood lipid profiles	Vegetarian diet	↓ HDL↑ TC ↑ LDL / HDL Ratio in premenopausal ♀. ↓ HDL↓ TC in postmenopausal ♀.
Jian et al.	2015	3257♀ 3551♂	15	1 year	Cholesterol levels	Vegetarian diet	↓ LDL in ♂ ↓ HDL in ♂ and in ♀
Chuang et al.	2016	4109	>20	1994-2008	Hypertension	Vegetarian diet	↓ Risk for hypertension by 34% (OR: 0.66, 95% CI: 0.50-0.87) ↓ SBP (-3.3mmHg, *p*<0.001) ↓ DBP (-1.5mmHg, *p*<0.001)
Kuchta et al.	2016	42	23-38	22 month	Lipid risk factors for atherosclerosis	Vegetarian diet	↓ TC (*p*<0.001) ↓ LDL (*p*<0.001) ↓ non-HDL-C (*p*<0.001) ↓ ApoB (*p*<0.001) ↓ apoB / apoA ratio (*p*<0.01)

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
Ho et al.	2017	269	40	March 2013 - October 2013	Blood pressure	Ovo-vegetarian diet	↓ SBP (119.0 mm Hg, SD¼ 15.82) ↓ DBP (125.1 mm Hg, SD¼ 18.91)
Shah et al.	2018	100	53-68	March 2014 - February 2017	Coronary Artery Disease	Vegetarian diet	↓ CRP by 32% (*p*=0.02).
Djekic et al.	2020	31	>18	September 2017 - March 2018	Coronary Artery Disease	Ovo-lacto-vegetarian diet	↑ Triacylglycerols with long-chain polyunsaturated fatty acyls ↓ Triacylglycerols with saturated fatty acyls.
Saintila et al.	2020	149	17-59	NR	Blood pressure	Vegetarian diet	↑ SBP (105.44 mm Hg) in the vegetarian ♀ than in the nonvegetarian ♀ (99.84 mm Hg). ↓ SBP (71.11 mm Hg) in the vegetarian ♂ than in the nonvegetarian ♂ (77.50 mm Hg). ↑ LDL (115.65 mg / dL) in Vegetarian ♀ compared to nonvegetarian ♀ (100.53 mg / dL)

CRF, cardiovascular risk factors; **CVDs**, cardiovascular diseases; **BMI**, body Mass Index; **SBP**, systolic blood pressure; **DBP**, diastolic blood pressure ; **TG**, triglycerides; **TC**, total cholesterol; **HDL**, High Density Lipoproteins ; **LDL**, Low Density Lipoproteins ; **Apo A**, apolipoprotein A ; **Apo B**, apolipoprotein B ; **cIMT**, carotid intima–media thickness; **ROM**, reactive oxygen metabolite ; **MS**, Metabolic syndrome; ♂, men; ♀, women; **OR**, odds ratio; **CI**, confidence interval; **CRP**, C reactive protein; **non-HDL-C**, non-high density lipoprotein cholesterol; **NR**, not reported; ↑ , Increase; ↓ , Decrease.

Table 6 Summary of characteristics of included studies that evaluate the effect of the Portfolio diet

Study	Year	patients	Age	Duration	Events	Diet included	Outcomes
David J.A. Jenkins et al.	2002	13	43-84	4 weeks	hyperlipidemia	Portfolio diet	↓ LDL by 29% ↓ Apo B de 24.2% ↓ TC/HDL Ratio by 19.8% ↓ LDL/HDL ratio by 26.5% ↓ Apo B/Apo A by 19.7%
David J.A Jenkins et al.	2003	25	36-85	4 weeks	hyperlipidemia	Portfolio diet	↓ Body weight ↓ LDL by 35.0% ↓ LDL/HDL ratio by 30.0%
D. J. Jenkins et al.	2005	34	36-71	4 weeks	hyperlipidemia	Portfolio diet	↓ LDL by -29.6 % No significant difference between the Portfolio regimen and statin therapy.
D. J. Jenkins et al.	2006	66	32-86	1 Year	Hypercholesterolemia	Portfolio diet	A mean LDL-cholesterol of ↓ 12.8 %
Gigleux et al.	2007	34	58	4 weeks	hyperlipidemia	Portfolio diet	↓ LDL-cholesterol <25.5 nm (-0.60 mmol/l)
David J.A. Jenkins et al.	2008	42	32-86	80 weeks	hyperlipidemia	Portfolio diet	↓ LDL of 15.4% ↓ LDL of 9.0% After elimination of plant sterols.
D. J. Jenkins et al.	2011	345	55-57	24 weeks	hyperlipidemia	Portfolio diet	↓ LDL -15.5%, for intensive dietary portfolio. ↓ LDL -15.0%, for routine dietary portfolio. ↓ DBP of 2.1 mm Hg, for intensive dietary portfolio. ↓ Risk of coronary heart disease

Study Year patients Age Duration Events Diet included Outcomes

Braun	2012	345	NR	6 month	hyperlipidemia	Portfolio diet	↓ LDL by 13.8% (*p*<0.001)
D.J.A. Jenkins et al.	2015	241	20-85	24 weeks	Blood pressure	Portfolio diet	↓ SBP of 2.1 mmHg ↓ DBP of de 1.8 mmHg ↓ Risk of coronary heart disease 1.2%. ↓ TC 0.7 mmol /L, ↓ Apo B of 0.2 g/L
Ramprasath et al.	2014	351	54-57	24 weeks	hyperlipidemia	Portfolio diet	↓ LDL levels (*p*<0.001) ↓ β-carotene, with intensive and routine dietary portfolio. ↑ γ-tocopherol, for routine dietary portfolio. ↑ Campesterol ↑ β- sitosterol, with intensive and routine dietary portfolio.
Richard & Joyner.	2019	NR	29 ♂	10 month	Hypercholesterolemia	Portfolio diet	↓ TC from 207 mg / dL to 142 mg/dL ↓ LDL from 135 mg/dL to 76 mg/dL.

LDL, Low Density Lipoproteins; **Apo B**, apolipoprotein B; TC, total cholesterol; **HDL**, High Density Lipoproteins; **Apo A**, apolipoprotein A; **DBP**, diastolic blood pressure; **SBP**, systolic blood pressure; ♂, men; **NR**, not reported; ↑ , Increase; ↓ , Decrease.