

Effects of Olive Oil Supplementation on Reducing the Risk of Cardiovascular Disease: A Scoping Review

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Abstract. Background The prevalence of cardiovascular disease is increasing in Indonesia. Cardiovascular disease ranks first among the causes of mortality in the world. Controlling the risk of cardiovascular disease becomes an effort to prevent the disease incidence. Previous studies have shown that olive oil has cardioprotective potential and reduces complications of cardiovascular disease. Objective: This is a scoping review which aims to identify the effects of olive oil on reducing the risk of cardiovascular disease. Methods: This research is a scoping review with search, selection, and analysis methodology being in accordance with the standards and using appropriate keywords. The scoping review articles came from the PubMed, Google Scholar, ScienceDirect, EBSCO, Directory of Open Access Journals, and Garuda Portal databases. The studies were assessed using the eligibility criteria from the PRISMA flow diagram. The articles used were those published in national and international journals in the period of 2010-2020 and available in full text. Results: The search results in 18 research articles that fulfill the criteria. Several studies significantly show that olive oil supplementation has cardioprotective properties through reduction of the risk of cardiovascular disease incidence and prevention of cardiovascular disease complications. The risk of cardiovascular disease can be reduced by reducing inflammatory markers, improving lipid profiles, or decreasing atherosclerosis. Conclusion: Olive oil has the potential to reduce the risk of cardiovascular disease by reducing inflammatory markers, improving lipid profiles, or reducing atherosclerosis.

Keywords: Olive Oil \cdot Cardiovascular Risk \cdot Cardiovascular Disease

1 Introduction

Cardiovascular disease is a major problem worldwide as it becomes the leading cause of death globally, reaching approximately 17.9 million individuals each year. The most frequent deaths from cardiovascular disease are caused by coronary heart attack and stroke. In Indonesia, cardiovascular disease is also a major cause of morbidity and mortality and responsible for one third of all deaths in Indonesia [1][2].

Cardiovascular disease results from impaired function of the heart and blood vessels, such as coronary heart disease, heart failure, hypertension, and stroke. The risk factors can include hypertension, dyslipidemia, diabetes, insulin resistance, and smoking. The most important factors underlying the incidence of cardiovascular disease are degenerative processes, inflammation, and thrombosis, which underlie vascular atherogenic changes. This disease can be prevented by having a healthy lifestyle, including diet [3][4].

Natural supplements are frequently used to prevent cardiovascular disease. One product that has long been consumed globally is olive (Olea Europaea), especially olive oil. Olive is a plant with numerous benefits for society, be it in the form of fruit, leaves, or oil. Olive oil is more popular among the public compared to the tree. It is often used as a healthy alternative to cooking oil. There are five types of olive oil, including 1) Extra Virgin Olive Oil/EVOO (produced from the first press, having an acidity degree of less than 1%), 2) Virgin Olive Oil/VOO (similar to extra virgin olive oil but taken from ripe fruit, having a higher acidity), 3) Refined Olive Oil/ROO (from refining, having an acidity degree of more than 3.3%), 4) Pure Olive Oil (having lighter aroma and taste than virgin olive oil), and 5) Extra Light Olive Oil (mixed from pure and refined oil, relatively popular due to the affordability) [5][6].

Olive oil is an important component of the Mediterranean Diet (MedDiet), being a major source of vegetable fats, particularly monounsaturated fatty acids (MUFA). Olive oil is also a good source of polyphenols which provide protection to the cells of the body from the damage caused by free radicals. Some of the beneficial effects of olive oil for health are the oleic acid content found in all types of olive oil and the more than 200 minor components which mainly include phenols, tocopherols, phytosterols, carotenoids, luteolin, and triterpenic acids [5][7][8].

Previous in-vitro and in-vivo studies with either preclinical or clinical trials suggest that olive oil has many health benefits as an anti-inflammatory, antithrombotic, antihypertensive, anti-aging, anti-diabetic, cardioprotective, antibacterial, antifungal, anti-hyperlipidemic, neuroprotective, and anti-cancer agent [9][10][11][12]. The cardioprotective effects of olive oil likely appear through several mechanisms, including antioxidant effects, anti-inflammatory effects, prevention of atherosclerotic process, improvement of dyslipidemia, antithrombotic effects, and reduction of blood pressure.

Research on the mechanisms of olive oil effects on reduction of the risk of cardiovascular disease remains unclear. Previous research by Rus et al. (2020) suggests that the antioxidant effects of Extra Virgin Olive Oil/EVOO can reduce the risk of thrombosis, inflammation, atherosclerosis, and oxidative stress. Olive oil, especially EVOO, has beneficial effects on cardiovascular risk factors, such as coagulation, platelet aggregation, lipids, endothelial function, and inflammation [13][14][15]. Previous studies have shown that consuming EVOO can lower inflammatory biomarkers, decrease the incidence of atherosclerosis and cardiovascular disease, and reduce complications. Syamsu et al. (2017) describe that olive oil has the ability to lower lipid profiles (total cholesterol, LDL, and triglyceride levels) and increase HDL levels in the blood of white rats (Rattus norvegicus) given a high-fat diet [16][17]. Based on the aforementioned background, this study aims to identify the effects of olive oil supplementation on the reduction of the risk of cardiovascular disease.

2 Method

This study is a scoping review with a standardized search, selection, and analysis methodology using the keywords "Olive oil", "Mediterranean diet", with "Cardioprotective", "antithrombotic", "hypolipidemia", "hypertension", "inflammatory", and "high risk cardiovascular risk". The scoping review articles were collected from the PubMed, Google Scholar, ScienceDirect, EBSCO, Directory of Open Access Journals, and Garuda Portal databases. This study was assessed using the eligibility criteria in the PRISMA flow diagram. The inclusion criteria were articles published in national and international journals in between 2010 and 2020, using Indonesian or English, and available in full text. The exclusion criteria were articles not available in full text for free. The search results using the aforementioned keywords resulted in 807 journals. Then, an analysis of article duplication was conducted based on the inclusion and exclusion criteria, resulting in 37 articles. In addition, the journal search was done manually by reading the title and abstract to match the topic, and the search was redone according to the predetermined criteria. Finally, there were 18 journals selected to be reviewed.

3 Result and Discussion

The procedure of article selection was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram [17]. The search flow diagram can be seen in Fig. 1.



Fig. 1. Flow Diagram of Data Search and Extraction

The final results of the search were 18 research articles that fulfilled the criteria. Several studies have significantly indicated that olive oil supplementation has cardioprotective properties by reducing the risk of cardiovascular disease incidence and preventing cardiovascular disease complications. The risk of cardiovascular disease can be reduced by lowering inflammatory markers, improving lipid profiles, or reducing atherosclerosis. The complete data is provided in Table 1.

No	Researchers	Title	n (Total)	Methods	Results
1	Guasch-Ferre et al (2020) [18]	Olive Oil Consumption and Cardiovascular Risk in U.S. Adults	61,181 women and 31,797 men	Cohort (24 years follow up)	circulating inflammatory biomarkers and a better lipid profile. risk of CVD
2	Estruch et al (2018) [19]	Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts	7447 participants (55 to 80 years of age, 57% women)	Randomized Clinical trial, multicenter (4,8 years follow up)	incidence of major cardio-vascular events Persons at high cardiovascular risk
3	Tee Khaw et al (2017) [20]	Randomized trial of coconut oil, olive oil or butter on blood lipids and other cardiovascular risk factors in healthy men and women	94 healthy men and women	Randomized Clinical trial, Placebo controlled (4 weeks follow up)	LDL-C on butter compared with coconut oil and with olive oil, (P<0.0001), no differences in change of LDL-C in coconut oil compared with olive oil (P=0.74)
4	Rus et al (2020) [13]	Effects of Olive Oil Consumption on Cardiovascular Risk Factors in Patients with Fibromyalgia	30 patients with Fibromyialgia	A randomized, controlled, double-blind nutritional trial (2 weeks follow up)	ROO - mean platelet volume and ⁻ platelet distribution width (PDW), neutrophil-to-lymphocyte ratio, ESR and fibrinogen (all p < 0.05). Consumption of olive oil may have antithrombotic and antiinflammatory
5	Luna RM et al (2012) [21]	Olive Oil Polyphenols Decrease Blood Pressure and Improve Endothelial Function in Young Women with Mild Hypertension	23 patients hypertension (women)(24-27 years old)	double-blind, randomized, cross-over (2 month follow up)	7.91 mm Hg in systolic, and 6.65 mm Hg of diastolic BP. serum asymmetric Dimethylarginine (AdMA), oxidized low density lipoprotein and plasma c-reactive protein (cRP)
6	Castillejo et al (2016) [22]	Polyphenol Rich Olive Oils improve Lipoprotein Particle Atherogenic Ratios and Subclasses Profile: A Randomized, Crossover, Controlled Trial	33 hypercholesterolemic individuals	a randomized, double-blind, crossover, controlled trial (3-weeks intervention)	The total LDL particle/total HDL article (HDL-P), small HDL/large HDL, and HDL-cholesterol/HDL-P ratios, and ⁻ lipoprotein insulin resistance index (LP-IR) (P<0.05).

Table 1. Summary of the articles reviewed

(continued)

No	Researchers	Title	n (Total)	Methods	Results
7	Guasch-Ferré et al (2014) [7]	Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study	7,216 men and women at high cardiovascular risk, aged 55 to 80 years	Multi center, Randomized Clinical trial, controlled double blind, (4.8 years follow up)	risk of cardiovascular mortality. Each 10 g/d increase dose, cardiovascular disease and mortality risk by 10% and 7%.
8	Casas et al (2014) [23]	The effects of the Mediterranean diet on biomarkers of vascular wall inflammation and plaque vulnerability in subjects with high risk for cardiovascular disease. A randomized trial.	164 participants at high risk for cardiovascular disease	A Randomized Trial	MD+EVOO and MD+Nuts showed a systolic (6 mmHg) and diastolic (3 mmHg) blood pressure (P = 0.02; both), as well as a LDL-cholesterol (P = 0.04), inflammatory biomarker: 34% in CD40 expression, CRP and interleukin-6, sICAM and Pselectin
9	Hernaez et al (2015) [24]	Olive Oil Polyphenols Decrease LDL Concentrations and LDL Atherogenicity in Men in a Randomized Controlled Trial1	25 healthy European men, aged 20–59 y	a randomized, cross-over controlled trial (3-week intervention)	The consumption of olive oil polyphenols plasma LDL concentrations and LDL atherogenicity in healthy young men.
10	Casas et al (2017) [25]	Anti-Inflammatory Effects of the Mediterranean Diet in the Early and Late Stages of Atheroma Plaque Development	66 (men and women) patients with high risk cardiovascular disease. 55-80 years old	Substudy PREDIMED. a 5-year, parallel-group, singleblind, multicenter, randomized, controlled feeding trial conducted	Long-term MeDiet the inflammatory biomarkers (IL-1 β , IL-5, IL-7, IL-12p70, IL-18, TNF- α , IFN- γ , GCSF, GMCSF, and ENA78) related to different steps of atheroma plaque development in elderly persons at high cardiovascular risk.
11	Khandouzi et al (2020) [26]	Effects of canola or olive oil on plasma lipids, lipoprotein-associated phospholipase A2 and inflammatory cytokines in patients referred for coronary angiography	48 patients (44 men and 4 women, aged 57.63 ± 6.34 years) with risk cvd	randomized, controlled, parallel-arm, clinical trial	Consumption of olive oil is more effective in the level of IL-6, whereas canola oil was more effective in lowering Lp-PLA2
12	Hadju et al (2012) [14]	Effects of Extra Virgin Olive Oil Supplementation on Total Cholesterol and Triglycerides Hypercholesterolemic Subjects.	11 women hypercholesterolemia	experimental, pre and post intervention (6 weeks)	total cholesterol after 6 weeks intervention, not decrease in triglyceride levels.

Table 1. (continued)

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No	Researchers	Title	n (Total)	Methods	Results
13	Casa et al (2016) [27]	Long-Term Immunomodulatory Effects of a Mediterranean Diet in Adults at High Risk of Cardiovascular Disease in the PREvencion' con Dleta MEDiterranea (PREDIMED)' Randomized Controlled Trial	160 subjects completed the study, including 74 men (55–80 y of age) and 86 women (60–80 y of age) who were free of CVD	Sub study a parallel-group, single-blind, multicenter, randomized, controlled 5-y clinical trial c	The MedDiet inflammatory markers related to atherosclerosis at 3 and 5 y hSCRP, IL-6,TNF a, and monocyte chemoattractant protein 1
14	Domenech M et al (2014) [28]	Mediterranean Diet Reduces 24-Hour Ambulatory Blood Pressure, Blood Glucose, and Lipids	We enrolled 284 consecutive subjects men aged 55 to 80 years and women aged 60 to 80 years at high cardiovascular risk but with no CVD at enrollment	a nutritional intervention trial with a randomized, 3-arm, parallel design	In high-risk individuals, MedDiets supplemented with extra virgin olive oil or nuts 24-hour ambulatory BP, total cholesterol, and fasting glucose.
15	Widmer et al (2013) [29]	Beneficial effects of polyphenol-rich olive oil in patients with early atherosclerosis	Eighty-two patients with early atherosclerosis (presence of endothelial dysfunction)	double-blind, randomized trial (4 months)	Improvement in endothelial dysfunction in patients with early atherosclerosis in association with significant in leukocytes
16	Mitjavila et al (2013) [30]	The Mediterranean diet improves the systemic lipid and DNA oxidative damage in metabolic syndrome individuals. A randomized, controlled, trial	110 female MetS (38 MedDiet þ VOO group, 35 MedDiet þ Nuts group and 37 Control diet group)	a large, parallel group, multicenter, controlled clinical trial (1 year follow up) Substudy Predimed	MedDiet oxidative damage to lipids and DNA in MetS individuals
17	Bendinelli Et al (2010) [31]	Fruit, vegetables, and olive oil and risk of coronary heart disease in Italian women: the EPICOR Study1–3	29,689 women (15,860 premenopausal and 13,829 postmenopausal)	Cohort prospective (7.85 years follow up)	An inverse association between increasing consumption of leafy vegetables and olive oil and CHD risk.
18	Perona et al (2011) [32]	Olive oil phenols modulate the triacylglycerol molecular species of human very low-density lipoprotein. A randomized, crossover, controlled trial	33 healthy volunteers (from 23 to 91 years old, with a regular lifestyle and dietary habits)	A placebo-controlled, double-blind, crossover, randomized, supplementation trial (3 weeks)	the significant dose-dependent linear trend between the PC in the olive oils and the palmitic and linoleic acid and their corresponding triacylglycerol molecular species in VLDL.

Table 1. (continued)

4 Discussion

From the search results in this study, 18 articles were found to meet the inclusion and exclusion criteria. They consist of randomized clinical trials and cohort studies. The research subjects are healthy individuals and individuals at risk of cardiovascular disease, such as hypertension, hyperlipidemia, and atherosclerosis. The age of the research subjects ranges from 24 to 80 years. Olive oil is given in the form of EVOO, ROO, or as part of the Mediterranean diet. The treatment duration using olive oil supplementation also varies from 3 weeks to 24 years. Although the research outputs vary, they are all associated with the risk of cardiovascular disease, reduction of inflammatory markers, and improvement of lipid profiles.

Previous in-vivo and in-vitro studies have shown that olive oil consumed as the main part of the Mediterranean diet has the antioxidant, anti-inflammatory, and anti-thrombotic potential. Therefore, olive oil consumption is potentially beneficial to main-tain the health of the body, especially to reduce the risk of cardiovascular disease. The use of which type of olive oil, the doses administered, and the duration of administration in these 18 articles vary greatly, thereby possibly affecting the variety of the results. However, in general, it can be seen that olive oil has the potential to reduce the risk of cardiovascular disease. From the data of the 18 articles, a summary of the effects of olive oil in reducing the risk of cardiovascular disease is presented in Table 2.

No	Effects of olive Oil on Cardiovascular Disease Prevention	Supporting Articles (References)
1	Preventing cardiovascular disease (myocardial infarction, heart failure, cardiac arrest, stroke)	[7][19][31]
2	Improving lipid profiles (decreasing total cholesterol, LDL, triglycerides, increasing HDL cholesterol)	[12][18][20][22][24][28][32]
3	Anti-inflammatory effect (reducing inflammatory markers)	[18][21][23][25][26][27][29][30]
4	Lowering blood pressure	[21][23][28]
5	Anti-thrombotic effect	[13]
6	Anti-oxidant effect	[30]

Table 2. Effects of Olive Oil on the Prevention of Cardiovascular Disease

The endpoint of reducing the risk of cardiovascular disease in these studies is apparently the reduction of cardiovascular incidence instead of control [7][19][31]. There are three articles with the endpoint being a decrease in inflammatory markers, seven articles have the endpoint of improving lipid profile, the endpoint of three articles is lowering blood pressure, and the anti-inflammatory effect of olive oil is supported by 8 articles. The anti-inflammatory effect can be seen from the decrease in the inflammatory biomarkers, such as CRP, IL-6, IL-1b, TNF, MCP1, and IFN. The process of inflammation is among the processes responsible for vascular changes which can lead to cardiovascular disease. The oleic acid of olive oil is able to protect vascular smooth muscle cells from apoptosis induced by prooxidant/proinflammatory mediators, and consumption of olive oil can reduce cardiomyocyte apoptosis. The anti-inflammatory and cardioprotective effects of EVOO are largely due to the high content of polyphenol molecules [5][15].

The administration of olive oil can improve lipid profiles by lowering the total cholesterol and LDL cholesterol levels as well as increasing HDL cholesterol [20][22][23]. Hypercholesterolemia can cause oxidative stress, which is characterized by an increase in Reactive Oxygen Species (ROS) in the body as well as a decrease in the anti-oxidant capacity. Oxidative stress per se can also deteriorate hypercholesterolemia. Extra virgin olive oil contains substances which can act as antioxidants and natural hypolipidemic compounds. Olive oil increases the antioxidant activity of hepatic enzymes, such as catalase, superoxide dismutase, and glutathione peroxidase. Hydroxytyrosol and oleuropein can act as free radical scavengers and inhibit the oxidation of low density lipoprotein (LDL). Squalene also lowers HMG CoA reductase activity and enhances the elimination of cholesterol through feces [14].

One of the cardioprotective effects of olive oil is a decrease in blood pressure. Three articles support the antihypertensive effect of olive oil in humans [21][23][28]. Based on previous studies, the antihypertensive effect is exerted through the mechanism of antioxidant activity, such as changes in aminopeptidase activity favoring Ang-2 production, an increase in endothelial nitric oxide synthase (eNOS) expression, and reduction in plasma Ang II. The OO polyphenols found in human serum after consumption of EVOO can decrease the endothelial activity and NADPH oxidase expression as demonstrated by decreased intracellular ROS levels and reduced expression and activity of MMP-2 and MMP-9 in the endothelial cells and adipocytes [30][33].

5 Conclusion

Based on the discussion, it is acknowledged that olive oil has the potential to reduce the risk of cardiovascular disease. This risk reduction occurs through anti-inflammatory mechanisms by reducing inflammatory markers, improving lipid profiles, lowering blood pressure, and exerting anti-thrombotics and antioxidants. This scoping review, however, has some limitations in that there is no standard treatment in each article since the olive oil dose is widely varied, the administration durations are different, and the subjects have various criteria. The molecular mechanisms and bioactive components of olive oil should be further studied. It also is necessary to conduct further clinical trials to verify the effects of olive oil on the reduction of cardiovascular risks by improving the study design, controlling the treatment in terms of both the dose and duration of administration, minimizing the confounding factors, and controlling the research subjects.

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