

The health benefits of olive oil in cardiovascular disease prevention: An update

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Olive oil is a key component of the Mediterranean diet, a dietary pattern with numerous health benefits that is regarded as a cornerstone in the prevention of metabolic, cardiovascular, and neurodegenerative diseases¹⁻³.

The first observations regarding the health benefits of the Mediterranean diet came from the pivotal Seven Countries Study, where a striking difference in death rates among studied cohorts was found; that difference remained significant even after adjusting for several known risk factors, like smoking, age, blood pressure and serum cholesterol. An increased consumption of mono-unsaturated fats (MUFAs), mostly oleic acid contained in olive oil, was negatively associated with death rate⁴. This was an observational study that, by nature, was unable to prove causality. Since then, several underlying mechanisms and metabolic pathways responsible for the favorable effects of olive oil, especially extra virgin olive oil, have been elucidated^{1,5-7}.

The chemical composition of olive oil is complex and depends on the circumstances of its production. Some of its key ingredients include oleic acid and phenolic compounds such as hydroxytyrosol, tyrosol and oleu-

ropein^{2,8}. Extra virgin has the highest quality of olive oil grades, as defined by the International Olive Council. It is described as having a free acidity (percentage of free oleic acid $\leq 0.8\%$) along with some other organoleptic and chemical characteristics⁸. It is currently believed that the beneficial effects of extra virgin olive oil are attributed to the combination of MUFAs and phenolic compounds. MUFAs have been associated with reduction of inflammation and oxidative damage, improved endothelial function and favorable effects on blood lipids, glucose metabolism and insulin sensitivity⁸⁻¹⁰. Polyphenols of olive oil are molecules with one or more phenolic groups that reduce oxidative stress by acting as scavengers of free radicals¹¹. Furthermore, apart from this antioxidant effect, the benefits of phenolic compounds extend to their anti-thrombotic and anti-inflammatory actions^{6,7,12,13}. Current evidence suggests that the beneficial cardiometabolic actions of polyphenols include improvement of endothelial function and nitric oxide (NO) bioavailability, reduction of systolic and diastolic blood pressure, as well as reduction of oxidized low-density lipoprotein (oxLDL)^{8,11}. These antiatherogenic effects of olive oil have been attributed to its polar compounds and have been associated with the antagonism of the platelet-activating factor¹⁴. The protective effect of hydroxytyrosol against lipid oxidation has been accredited by the European Food Safety Authority

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(EFSA), which recommends the consumption of at least 5 mg of hydroxytyrosol and its derivatives per 20 g of olive oil daily¹⁵. Furthermore, positive effects of olive oil and its components have been reported in terms of weight loss and reduced incidence of metabolic syndrome and type 2 diabetes^{1,11,16}.

Several studies have provided intriguing results regarding the beneficial effects of olive oil consumption on metabolic and cardiovascular health. The PREDIMED, a multicenter trial conducted in Spain, enrolled 7447 participants at high cardiovascular risk¹⁷. These participants were randomly assigned to 3 different dietary patterns: a Mediterranean diet enriched with nuts, a Mediterranean diet enriched with extra virgin olive oil, or a control low fat diet. The primary endpoint was the composite of myocardial infarction, stroke and death from cardiovascular causes, and the median follow-up was 4.8 years. This trial was first published in 2013, but the publication was withdrawn due to protocol deviations regarding randomization. An amended analysis was published in 2017 in the same journal. The adjusted intention-to-treat analysis showed that the hazards ratios for the Mediterranean diet supplemented with extra virgin olive oil or nuts were 0.69 [95% confidence intervals (CI): 0.53-0.91] and 0.72 (95% CI: 0.54-0.91), respectively, compared with the control diet. The results were comparable when the subjects suspected to have deviated from the randomization protocol were excluded: HR: 0.66 (95% CI: 0.49-0.89) for the extra virgin olive oil, and 0.64 (95% CI: 0.47-0.88) for the nut-supplemented diet¹⁷.

A lower risk for cardiovascular disease and stroke associated with olive oil consumption was reported in a recent, secondary pooled analysis of 3 Spanish cohorts (AWHS, SUN Project and EPIC-Spain)¹⁸. A total of 59,977 participants were included and olive oil consumption was assessed with validated questionnaires. The greatest benefit was observed with a daily intake of 20-30 g of olive oil. Extra virgin grade was strongly associated with favourable outcomes.

Another study to assess the possible relationship between total olive oil consumption and mortality was recently published; this study included subjects from 2 large prospective cohorts from the United States. This is in contrast to most published studies that have included population from Mediterranean countries, where the consumption of olive oil is much higher¹⁹. The population consisted of 60,582 women and 31,801 men without history of cardiovascular disease or cancer, and the follow-up was 28 years. When the highest intake of olive oil (more than 7 g per day) was compared to rare or no intake, a 19% lower risk for total (HR: 0.81, 95% CI: 0.78-0.84) and cardiovascular disease mortality (HR: 0.81, 95% CI: 0.75-

0.87) was observed. Inverse associations were found for neurodegenerative disease (HR: 0.71, 95% CI: 0.64-0.78), cancer (HR: 0.83, 95% CI: 0.78-0.89), and respiratory disease mortality (HR: 0.82, 95% CI: 0.72-0.93). Substitution analyses showed that the replacement of 10 g per day of other types of fat (dairy fat, butter, margarine, mayonnaise) with olive oil would reduce the risk of total and cause-specific mortality by 8-34%.

In the recently published randomized CORDIOPREV study, a Mediterranean diet that included at least 4 tablespoons of extra virgin olive oil daily was compared with a low-fat diet in patients with established coronary heart disease¹³. The primary end point was a composite of myocardial infarction, revascularisation, ischaemic stroke, peripheral artery disease, and cardiovascular death, and the follow up was 7 years. The olive oil-enriched Mediterranean diet was associated with better prognosis, with HRs ranging from 0.719 (95% CI: 0.541-0.957) to 0.753 (0.568-0.998). These effects were more prominent in men. Interestingly, an analysis of the CORDIOPREV study reported that the Mediterranean diet decreased the intima-media thickness of both common carotid arteries (IMT-CC), as assessed by B mode ultrasound, at 5 years (-0.027 ± 0.008 mm, $p < 0.001$) and this effect was maintained at 7 years (-0.031 ± 0.008 , $p < 0.001$). The measurement of IMT-CC is a non-invasive method that is regarded as a surrogate marker for subclinical atherosclerosis²⁰. These findings are important as they extend the benefits of the Mediterranean diet to the secondary prevention setting.

Health benefits of olive oil, especially extra virgin one, are further supported by findings of recently published studies. The totality of data reinforces the recommendation of olive oil consumption in the context of a Mediterranean diet.

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Conflicts of interest

The authors report no conflicts of interest

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