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**File: ■ Olive (*Olea europaea*, Oleaceae) Oil  
■ Thyme (*Thymus vulgaris*, Lamiaceae)  
■ Lipoprotein Profiles  
■ Atherogenic Ratios**

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**RE: Olive Oils Enriched with Olive or Thyme Polyphenols Improve Lipoprotein Profiles and Atherogenic Ratios**

Fernández-Castillejo S, Valls RM, Castañer O, et al. Polyphenol rich olive oils improve lipoprotein particle atherogenic ratios and subclasses profile: a randomized, crossover, controlled trial. *Mol Nutr Food Res*. July 2016;60(7):1544-1554.

Research has shown that polyphenol-rich foods improve lipid profiles and cardiovascular disease risk. Both thyme (*Thymus vulgaris*, Lamiaceae) and olive (*Olea europaea*, Oleaceae) oil are rich in polyphenols and may provide cardiovascular health benefits. Lipid profiles analyzed by nuclear magnetic resonance (NMR) may be better for predicting atherosclerosis risk than conventional methods. The aim of this randomized, double-blind, crossover, controlled trial was to assess the effect of 2 functional olive oils (1 enriched with olive polyphenols and the other with thyme polyphenols) by evaluating NMR lipoprotein profiles and atherogenic ratios.

This study took place at Institut Hospital del Mar d'Investigacions Mèdiques in Barcelona, Spain, from April to September 2012. Male and female patients with hypercholesterolemia (total cholesterol >200 mg/dL) were recruited from newspaper and university advertisements for this study. Patients were excluded from the study if they had low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL; triglycerides ≥350 mg/dL; fasting blood glucose >126 mg/dL; plasma creatinine levels >1.4 mg/dL for women and >1.5 mg/dL for men; body mass index >35; were smokers (>1 cigarette/day); were athletes with physical activity >3000 metabolic equivalent min/day; or had other conditions that would interfere with the study outcomes.

A total of 33 patients (19 men and 14 women) with hypercholesterolemia received 25 mL (22 mg)/day of either standard virgin olive oil (VOO), olive oil enriched with its polyphenols (FVOO, 500 ppm), or olive oil enriched with its polyphenols (250 ppm) and those of thyme (250 ppm) (FVOOT) (manufacturer unknown). The functional olive oils were administered randomly in 3 different sequences (3-week intervention periods, with 2-week washout periods before each intervention period) for each of the groups, and included the following: FVOO, FVOOT, VOO (sequence 1, n=11); FVOOT, VOO, FVOO

(sequence 2, n=11); and VOO, FVOO, FVOOT (sequence 3, n=11).

Measurements of 24-hour urinary biomarkers of FVOO (hydroxytyrosol-sulfate) and FVOOT (thymol-sulfate), before and after each intervention period, were evaluated to confirm adherence to the interventions. Furthermore, 3-day dietary records, physical activity, blood pressure, body measurements, and 24-hour blood samples were collected before and after each intervention period. Patients also were advised to consume a low-polyphenol diet. Changes in lipoprotein particle atherogenic ratios and subclasses (based on NMR data), as well as glucose, total cholesterol, and classic lipid profiles, were evaluated from blood samples.

Only 1 patient in each sequence did not finish the intervention. No adverse effects were reported, and no significant differences were observed at baseline. Daily energy expenditure remained the same during the study. No changes in blood pressure or body measurements were found. Biomarkers for both FVOO and FVOOT were significantly increased in accordance with the functional olive oil consumed ( $P < 0.05$ ). None of the interventions significantly altered glucose levels, classic lipid profiles, or apolipoprotein (Apo) concentrations, in comparison to VOO. One exception for the classic lipid profile was LDL-C, which was significantly lower after FVOO, in comparison to the other olive oils ( $P < 0.05$ ).

LDL particle (LDL-P) size, as well as changes in total LDL-Ps, intermediate-density lipoprotein particles, and total ApoB100-containing lipoproteins, decreased significantly more with FVOO than with the other interventions ( $P < 0.001$ ). Changes in small LDL-P concentrations were significantly decreased after FVOO interventions compared to the FVOOT intervention ( $P < 0.05$ ). Both functional olive oils promoted an increase in high-density lipoprotein particle (HDL-P) size and a decrease in medium very-low-density lipoprotein particles (VLDL-Ps) ( $P < 0.05$ ). FVOO intake led to the highest increase in HDL-P size ( $P < 0.05$ ) and the greatest decrease in small HDL-Ps ( $P < 0.05$ ). The VLDL-P size decreased after FVOO intervention ( $P < 0.05$ ).

The LDL-P/HDL-P ratio also significantly decreased after FVOO compared to the other olive oils ( $P < 0.05$ ). FVOO intake also led to a greater decrease in small HDL/large HDL (S-HDL/L-HDL) than FVOOT intake ( $P < 0.05$ ). Both functional olive oils decreased the HDL/HDL-P and S-HDL/L-HDL ratios, and the lipoprotein insulin resistance index (LP-IR) ratio ( $P < 0.05$ ).

The authors found that the 2 functional olive oils assessed in this study had beneficial effects on lipoprotein subclass distribution, the LP-IR, and the atherogenic ratios compared to the natural VOO. In particular, the functional oil enriched with polyphenols from olive oil had the most pronounced effects. The authors state, "To the best of our knowledge this is the first time that a decrease in these atherogenic ratios associated to a dietary intervention has been reported." This effect should be confirmed in larger trials that especially focus on olive oils enriched with olive oil polyphenols.

—*Laura M. Bystrom, PhD*

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