One year of Mediterranean diet decreases microvesicle release from activated platelets and leukocytes in asymptomatic high cardiovascular risk patients

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Background/Introduction
Microvesicles (MV) are small phospholipid-rich vesicles released into blood by cells that are either damaged, activated or apoptotic. MV participate in diverse functions and also can serve as biomarkers of ongoing cardiovascular cell instability and disease (CVD). Diet is one of cornerstones for CVD prevention, and the effects of diet on MV shedding are poorly characterized.

Purpose
We aimed at investigating the long term effects of a Mediterranean diet compared to a low fat diet (LFD) in MV shedding by cells of the vascular compartment in asymptomatic but high cardiovascular risk patients treated as per guidelines.

Methods
A total of 155 patients with diabetes or >3 cardiovascular risk factors but free of cardiovascular event were included in the study, consisting in a 3-arm randomized clinical trial. The interventions were as follows: a Mediterranean diet supplemented with extra-virgin olive oil -EVOO- (n=53); a Mediterranean diet supplemented with mixed nuts -NUTS- (n=49); and a control diet -LFD- (n=53) for one year. Subjects were matched by age, sex, diabetes and dyslipidaemia. At baseline and after one year follow-up, the number of MV and their phenotypic characteristics were assessed by flow cytometry. Phosphatidylserine exposure by annexin V (AV) binding was assessed and different monoclonal antibodies against characteristic cell epitopes were used to identify parental cell origin.

Results
The mean patient age was 66 years (50% males). Patients were hypertensive (>75%), diabetics (>50%) and dyslipidemics (>30%). No significant changes were observed after one year follow-up in body weight, body mass index, blood pressure, glucose, triglycerides, total, LDL and HDL cholesterol, medication or physical activity within or among groups of intervention.

Total MV (AV+/-) were present in higher concentration than AV+ MV for all analyzed phenotypes and cell origins (P<0.0001, all). After one year follow-up, in the EVOO group there was a significant decrease in the concentration of monocyte-derived (CD14+/AV+, CD14+/CD11a+/AV+) and smooth muscle cell-derived (SMA-a+/AV+) circulating MV. In the NUTS group there was a significant decrease in platelet-derived (PAC-1+/AV+, CD62P+/AV+, and CD61+/AV+) MV, and activated cells-derived (CD142+/AV+, CD11a+/AV+ and CD63+/AV+) MV concentrations. On the other hand, one year of LFD decreased platelet PAC-1+/CD62P+/AV+ and CD61+/AV+ MV release. Interestingly, after one year follow-up PAC-1+/AV+ and...
CD14+/CD11a+/AV+ MV were significantly different between both mediterranean diets compared to the LFD.

Conclusions
MV are liquid biopsy biomarkers of vascular- and blood-cell activation and injury, that appear sensitive to modification by diet. Therefore, our results indicate that following a mediterranean diet rich in nuts and EVOO clearly prevent cell activation towards a pro-atherosclerotic phenotype and therefore can delay the development of CV complications.