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707 - METABOLOMICS-BASED PREDICTION OF TYPE 2 DIABETES IN TWO INDEPENDENT HIGH-RISK POPULATIONS AND POTENTIAL MODIFICATION EFFECT BY AN INTENSIVE LIFESTYLE INTERVENTION

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Resumen

Background/Objectives: Biomarkers are increasingly recognized as valuable tools for the early prediction of disease, facilitating interventions aimed at delaying its onset and consequences. This study aimed to identify a plasma metabolomic risk score (MRS) corresponding to a metabolomic signature of type 2 diabetes incidence and whether a randomized lifestyle intervention with an energy-reduced Mediterranean diet (MedDiet) could attenuate the risk of type 2 diabetes predicted by this MRS.

Methods: A case-control study nested in the PREDIMED-Plus trial served as the discovery cohort assessing 570 candidate plasma metabolites to identify a MRS. The association between the MRS and type 2 diabetes risk was validated in an independent case-cohort study nested within another trial, the PREDIMED. Potential effect modification by the randomized lifestyle interventions conducted in both randomized trials, separately or combined, was also assessed.

Results: A 16-metabolite MRS was identified in the discovery cohort, including hexoses, aminoadipic acid, symmetric dimethylarginine, and lysophospholipids, with adjusted OR (95%CI) = 1.98 (1.73, 2.25) per SD. In the external validation cohort (in which 12 of the 16 metabolites were available), the MRS showed a strong association with type 2 diabetes [HR (95%CI) = 5.30 (3.92, 7.17) per SD]. This MRS modestly improved type 2 diabetes risk prediction beyond traditional clinical risk factors. A significant attenuation of the MRS-associated risk was observed among participants assigned to the randomized lifestyle intervention in PREDIMED-Plus when evaluating the 2-df interaction that jointly considered the PREDIMED-Plus and PREDIMED interventions (p = 0.0022).

Conclusions/Recommendations: A MRS predictive of type 2 diabetes incidence was identified and externally validated. The MRS added predictive value beyond classical risk factors. Its associated risk was attenuated through intensive lifestyle modification with an energy-reduced MedDiet.

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