

Prediagnostic Plasma Metabolomics and the Risk of Exfoliation Glaucoma

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PURPOSE: The etiology of exfoliation glaucoma (XFG) is poorly understood. We aimed to identify a prediagnostic plasma metabolomic signature associated with XFG.

METHODS: We conducted a 1:1 matched case-control study nested within the Nurses' Health Study and Health Professionals Follow-up Study. We collected blood samples in 1989-1990 (Nurses' Health Study) and 1993-1995 (Health Professionals Follow-up Study) . We identified 205 incident XFG cases through 2016 (average time to diagnosis from blood draw = 11.8 years) who self-reported glaucoma and were confirmed as XFG cases with medical records. We profiled plasma metabolites using liquid chromatography-mass spectrometry. We evaluated 379 known metabolites (transformed for normality using probit scores) using multiple conditional logistic models. Metabolite set enrichment analysis was used to identify metabolite classes associated with XFG. To adjust for multiple comparisons, we used number of effective tests (NEF) and the false discovery rate (FDR) .

RESULTS: Mean age of cases (n = 205) at diagnosis was 71 years; 85% were women and more than 99% were Caucasian; controls (n = 205) reported eye examinations as of the matched cases' index date. Thirty-three metabolites were nominally significantly associated with XFG (P < 0.05). **CONCLUSIONS:** In plasma from a decade before diagnosis, lysophosphatidylcholines and phosphatidylethanolamine plasmalogens were positively associated and triacylglycerols and steroids (e.g., cortisone) were inversely associated with XFG risk.

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