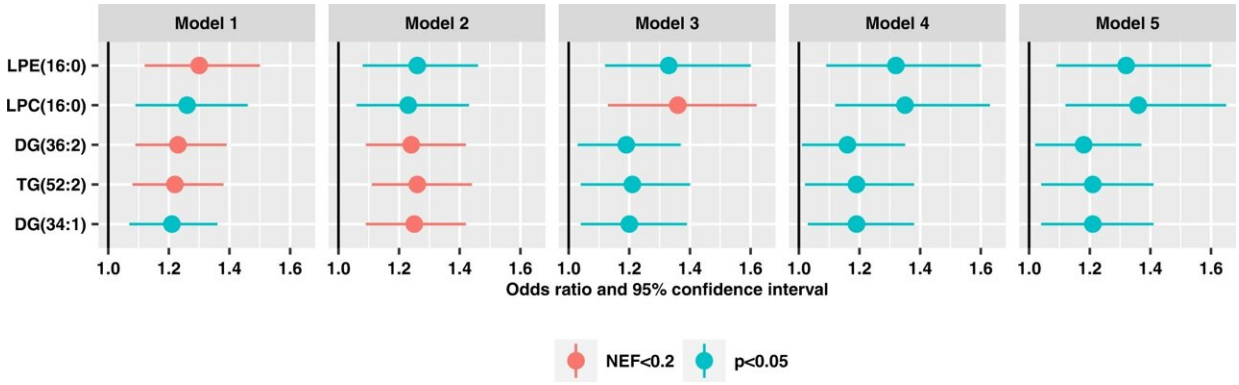
Higher levels of diglycerides and triglycerides adversely associated with glaucoma

June 13 2023



Individual metabolites among the n = 369 metabolites evaluated that were significant across the various nested multiple conditional logistic regression models of primary open-angle glaucoma (599 cases and 599 controls in NHS/NHSII/HPFS). Data are presented as odds ratios and 95% confidence intervals estimated with conditional logistic regression models. **Model 1**: basic model, adjusting for matching factors only (see Table 1); **Model 2** (factors that affect metabolite levels and matching factors as matching was imperfect): Model 1 plus age, gender, smoking status, BMI, physical activity, time of day of blood draw, month of blood draw, fasting status; **Model 3** (established risk factors for primary open-angle glaucoma (POAG)): Model 2 plus family history of glaucoma, socioeconomic index based on census tract data, race/ethnicity and age at menopause; **Model 4** (potential modifiable dietary risk factors for POAG): Model 3 plus nitrate intake, caffeine intake, alcohol intake, caloric intake; **Model 5** (systemic comorbidities/drugs suggested to be associated with POAG in some studies): Model 4 plus hypertension, high cholesterol, diabetes, and oral steroid use. LPC (16:0) and LPE (16:0) were assessed among women only. LPE lysophosphatidylethanolamine; LPC lysophosphatidylcholine; DG

diglyceride; TG triglycerides. Exact species can be found using the HMDB identification number listed in the supplement. All statistical tests are two-sided, and we accounted for multiple comparisons by using *p* values based on the number of effective (NEF) tests. Source data with exact values are provided as a Source Data file. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-38466-w

Glaucoma is the leading cause of irreversible blindness worldwide. Primary open-angle glaucoma (POAG) is the most common form, and yet the cause of this disease is poorly understood. Findings from previous genome-wide association studies suggest that there is a complex metabolic network that affects optic nerve health.

Researchers from Brigham and Women's Hospital, a founding member of the Mass General Brigham healthcare system, and the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai aimed to identify plasma metabolites associated with risk of developing POAG in a case-control study nested within the prospective Nurses' Health Studies and the Health Professionals Follow-Up Study.

This study included 599 participants who developed POAG and 599 matched controls and examined pre-diagnostic circulating plasma metabolites from approximately 10 years before POAG diagnosis.

To confirm the findings, the researchers evaluated the metabolomic data in plasma samples of 2,238 glaucoma cases and 44,723 controls from the UK Biobank. They found that higher levels of diglycerides and triglycerides were associated with risk of glaucoma, suggesting that they play an important role in glaucoma pathogenesis.

"Our study is the first to assess associations between pre-diagnostic

circulating metabolites and POAG risk in two large independent datasets," said co-first authors Oana A. Zeleznik, Ph.D., and Jae H. Kang, ScD, investigators at Brigham's Channing Division of Network Medicine.

"These results provide new insights into the etiology of POAG. Our data implicate dysregulation in lipid metabolism and mitochondrial function in glaucoma etiology and suggest new targets for glaucoma prevention or therapies," said senior author Louis R. Pasquale, MD, Professor of Ophthalmology at the Icahn School of Medicine at Mount Sinai.

The research is published in the journal *Nature Communications*.

More information: Oana A. Zeleznik et al, Plasma metabolite profile for primary open-angle glaucoma in three US cohorts and the UK Biobank, *Nature Communications* (2023). DOI: 10.1038/s41467-023-38466-w

Provided by Brigham and Women's Hospital