Circulating metabolic markers and risk of pancreatic cancer: a case-subcohort study

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Introduction

Pancreatic cancer has a very poor prognosis with 5-year survival of 5-10% and is often diagnosed late

Metabolic risk factors, such as adiposity and diabetes, and biomarkers, such as plasma glucose, fatty acids, and some proteins, have been shown to be associated with risk

Aimed to assess the associations between circulating metabolites and risk of pancreatic cancer

Methods

Case-subcohort study on 681 incident pancreatic cancer cases and a subcohort of 892 individuals within the China Kadoorie Biobank, a prospective study of 512,891 adults

225 metabolic biomarkers measured in baseline plasma samples using nuclear magnetic resonance (NMR)

Cox regression fitted using the Prentice pseudo-partial likelihood, stratified by sex and region and adjusted for age, age^2, time since last meal and its square, smoking status, alcohol consumption, educational attainment, diabetes, and body mass index, and time in study was used as the time scale

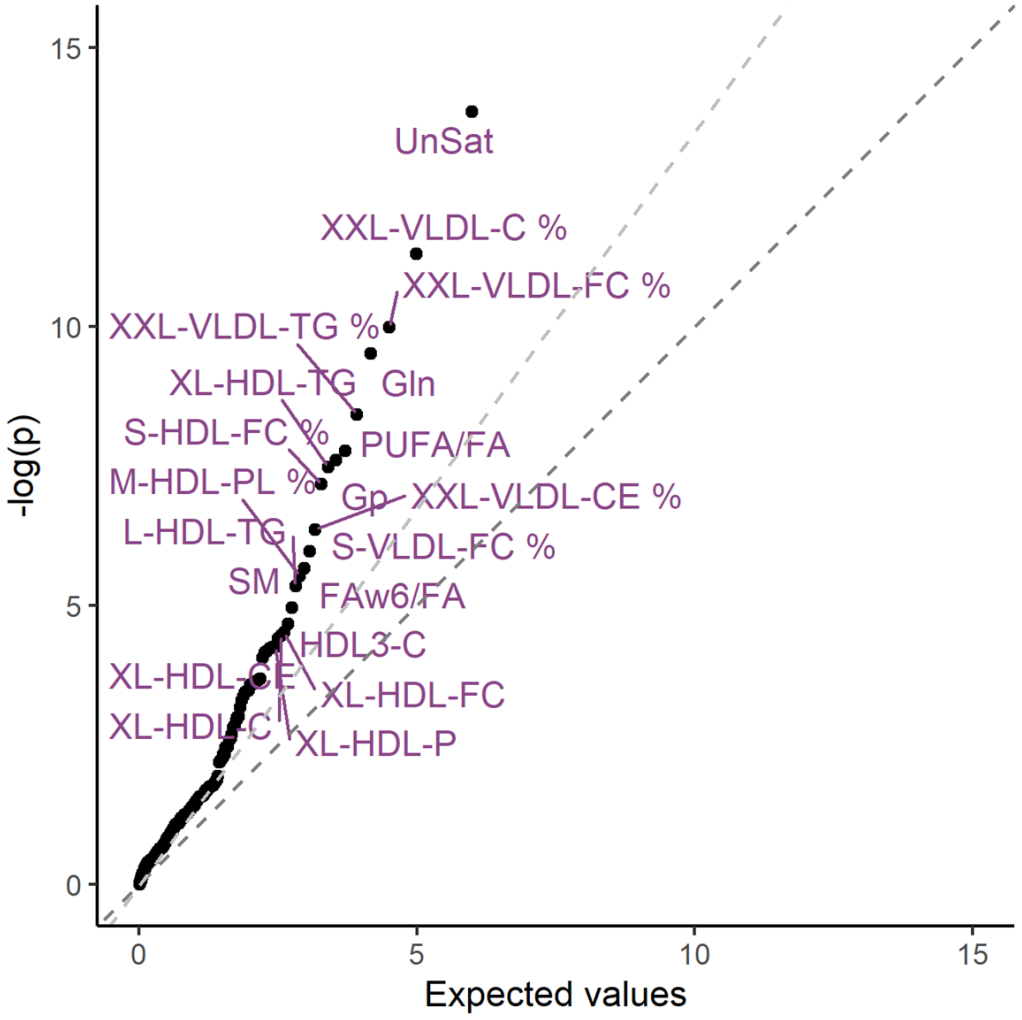
Associations with risk of pancreatic cancer

Several lipid-related biomarkers were associated with risk of pancreatic cancer, with adjusted HRs per 1-standard deviation increase in biomarker of 0.74 to 1.37

Glycoprotein acetyls and ratios of monounsaturated and of saturated fatty acids to total fatty acids were associated with a higher risk, while sphingomyelins, glutamine, estimated degree of unsaturation and ratios of omega-6 fatty acids and of polyunsaturated fatty acids to total fatty acids were associated with lower risk

The discriminatory ability of a model with known risk factors increased when several metabolic biomarkers were included (C-statistic 0.76 to 0.78)

Associations with risk of pancreatic cancer



UnSat: Estimated degree of unsaturation

XXL-VLDL-C %: Total cholesterol to total lipids ratio in chylomicrons and extremely large VLDL

XXL-VLDL-FC %: Free cholesterol to total lipids ratio in chylomicrons and extremely large VLDL

Gln: Glutamine

XXL-VLDL-TG %: Triglycerides to total lipids ratio in chylomicrons and extremely large VLDL

PUFA/FA: Ratio of polyunsaturated fatty acids to total fatty acids

Gp: Glycoprotein acetyls, mainly a1-acid glycoprotein

XL-HDL-TG: Triglycerides in very large HDL

S-HDL-FC %: Free cholesterol to total lipids ratio in small HDL

XXL-VLDL-CE %: Cholesterol esters to total lipids ratio in chylomicrons and extremely large VLDL

S-VLDL-FC %: Free cholesterol to total lipids ratio in small VLDL

FAw6/FA: Ratio of omega-6 fatty acids to total fatty acids

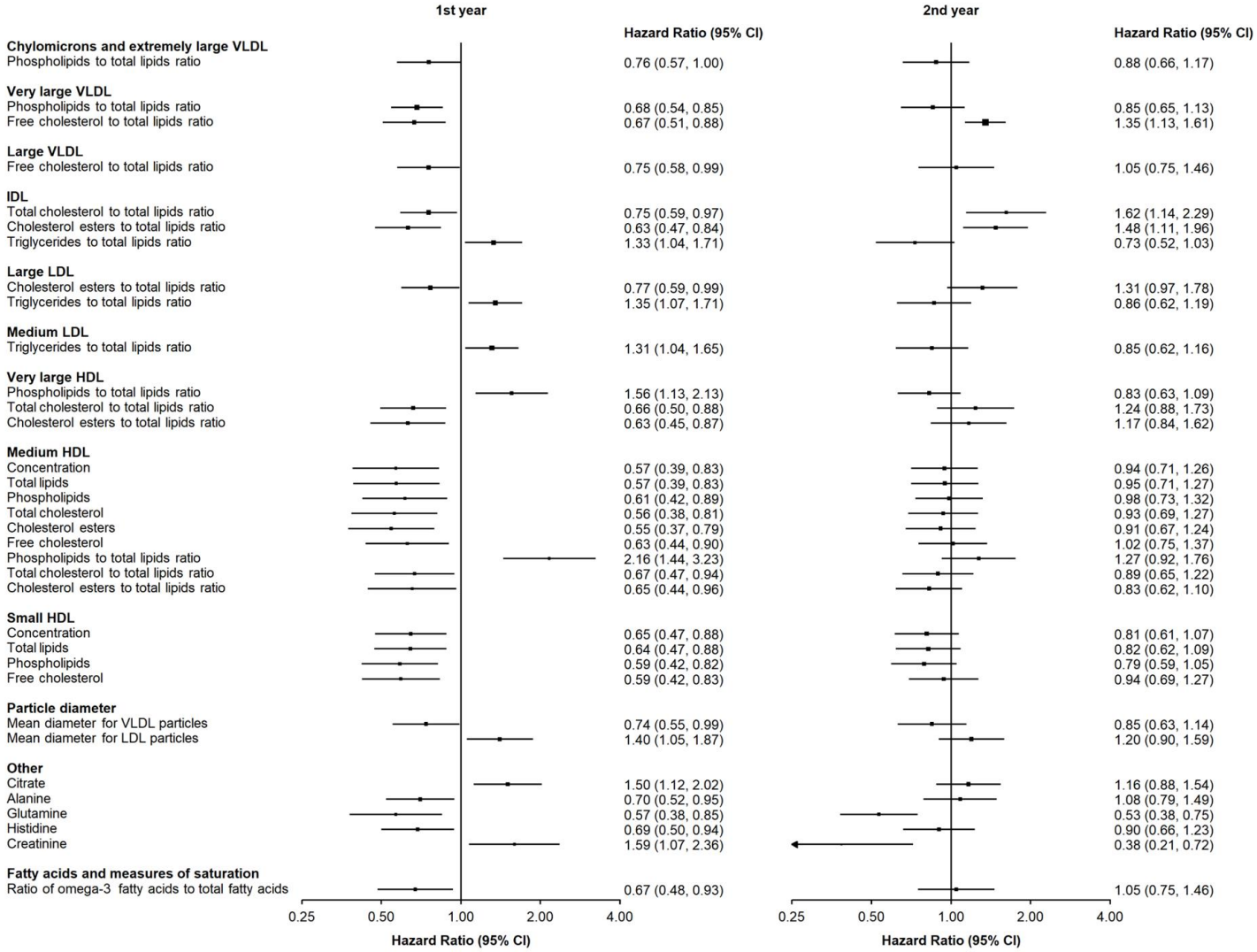
Associations with short-term risk

Among pancreatic cancer cases, 47 (6.9%) were diagnosed within a year from baseline (and therefore of blood collection), 53 (7.8%) at 1 to less than 2 years, 217 (31.9%) were diagnosed 2 to less than 5 years and 364 (53.5%) were diagnosed 5 years or more after blood collection

Associations between some biomarkers and risk of pancreatic cancer were time-varying; for example fractions of medium and small HDL were inversely associated with short-term risk (within the first year of follow-up)

Within the first year, discriminatory ability substantially increased when including metabolic biomarkers (C-statistic 0.88 to 0.94)

Associations with short-term risk



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Discussion

Several metabolic blood biomarkers were associated with short- and long-term risk of pancreatic cancer and may be useful to incorporate in strategies for prevention and earlier diagnosis

Our findings may provide insights into the pathophysiology of pancreatic cancer and future studies are needed to understand the role of these metabolic biomarkers in pancreatic cancer development

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