SCOTTISH SOCIETY FOR GASTROENTEROLOGY
Summer Meeting 2018

Poster Presentation

TITLE	**Does a common genetic polymorphism increase the susceptibility of developing alcoholic liver disease in patients with type 2 diabetes?**
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ABSTRACT DETAILS:	
Background:	Alcoholic liver disease (ALD) remains a major burden to health services accounting for 3.3 million deaths worldwide. Curiously, only a proportion of alcohol abusers develop symptomatic ALD, implying that the predisposition to this disease may be influenced by genetic factors. One candidate gene of interest is CYP2E1, as it is induced in response to chronic alcohol consumption, and has the ability to produce reactive oxygen species, a known contributor to ALD. However, genetic analysis of patients with various polymorphisms in CYP2E1 has, herein, been controversial. Here we report an exciting finding of a novel association between a common CYP2E1 single nucleotide polymorphism, rs9419079, and the propensity to develop ALD in a type 2 diabetes population.
Method:	The GoDARTS/MEMO databases are composed of data from patients with type 2 diabetes including prescribing, biochemistry, admissions and biophysical markers. Three cohorts were identified based upon their drinking status and conditions related to dangerous alcohol consumption: non-drinkers (n=7476), patients with alcohol abuse or dependence (n=107), and patients with alcoholic liver disease (n=187). Each cohort was linked to data regarding age, BMI, sex, HbA1c, serum triglycerides and rs9419079 polymorphism status. Heterozygotes and homozygous patients with rs9419079 polymorphism were presumed to exhibit phenotypic similarities and their data was therefore merged due to low frequency of homozygotes with rs9419079 polymorphism.
Results:	Patients with ALD were more likely to have at least one rs9419079 polymorphism when compared with non-drinkers (33.0% to 26.0%; $P < 0.05$) and patients who abuse alcohol or are dependent on alcohol (33.0% to 20.6%; $P < 0.05$). Multiple logistic regression demonstrated that the presence of at least one rs9419079 polymorphism was an independent risk factor for ALD (OR: 2.01, CI: 1.15-3.63; $P = 0.017$). Other risk factors included BMI (OR: 1.05 CI: 1.00-1.10; $P = 0.044$), and age (OR: 1.02, CI: 1.00-1.05; p=0.025).
Conclusions:	These findings strongly suggest that rs9419079 polymorphism is independently associated with the propensity to develop ALD in patients with type 2 diabetes mellitus. This suggests CYP2E1 plays a role in ALD susceptibility, and potentially identifies a novel ALD susceptibility polymorphism.
References:	Osna N, Donohue Jr T, Kharbanda K. Alcoholic Liver Disease: Pathogenesis and Current Management. Alcohol Res. 2017;38(2):147–61. WHO. Global status report on alcohol and health [Internet]. World Health Organisation. 2014. p. 1–5. Available from: http://www.who.int/mediacentre/factsheets/fs349/en/ Lieber CS. Microsomal Ethanol-Oxidizing System MEOS: The First 30 Years (1968-1998) - A Review. Alcoholism. 1999;23(6):991–1007. Zeng T, Guo F, Zhang C, Song F, Zhao X, Xie K. Roles of Cytochrome P4502E1 Gene Polymorphisms and the Risks of Alcoholic Liver Disease: A Meta-Analysis. PLoS One. 2013;8(1):1–8. Zintzaras E, Stefanidis I, Santos M, Vidal F. Do Alcohol-Metabolizing Enzyme Gene Polymorphisms Increase the Risk of Alcoholism and Alcoholic Liver Disease? Hepatology. 2006;43(2):352–61.