Alcohol consumption and smoking dose-dependently and synergistically worsen local pancreas damage

Chronic pancreatitis (CP) is characterised by irreversible damage to the pancreas causing endocrine and exocrine dysfunction which results in decreased quality of life and reduced life expectancy.[1]

Adam *et al* recently published an interesting study on a possible diagnostic tool for CP based on metabolomic profiles of patients and controls.[2]

Our previous international cohort analysis showed that the proportion of patients developing CP is exponentially and directly associated with the number of acute pancreatitis (AP) episodes, thus strengthening the focus on the challenging task of diagnosing CP early.[3 4] However, in addition to diagnosing early, we should also focus on preventive interventions, before the damage becomes irreversible.

Alcohol is the main aetiological factor for CP and both alcohol consumption and smoking increase the risk for recurrence of AP and the development of CP. According to Ahmed Ali *et al*, in a follow-up study of 669 AP patients, smoking represented the dominant risk factor for recurrent AP (RAP) and a combination of alcohol consumption and smoking was the main risk factor for the progression to CP.[5] Therefore, cessation programmes and patient education are extremely important means to intervening and lowering the recurrence of AP and the progression to CP.[6 7] However, total cessation and abstinence often seems impossible for patients and they do not even try. Is it also possible to reduce recurrence and progression by decreasing the amount consumed?

Basic research evidence clearly suggests that alcohol and smoking amplify each other's harmful effects.[8 9] However, large cohorts are lacking to determine whether smoking and alcohol consumption dose-dependently, mutually exacerbate the damage to the pancreas caused by each.

We have used the international cohort in the Acute Pancreatitis Registry initiated by the Hungarian Pancreatic Study Group. Data were collected from 13 countries and 30 medical centres, with 2441 cases included in the analysis. Further characteristics of the cohort and information on methods are available in online supplemental file 1.

The patient population was divided into groups according to current amounts of smoking and alcohol consumption. We found that both smoking and alcohol consumption are dose-dependently associated with amylase and lipase levels and with the prevalence of RAP and CP among AP patients. Alcohol consumption was also linked to a higher rate of local complications (figure 1).

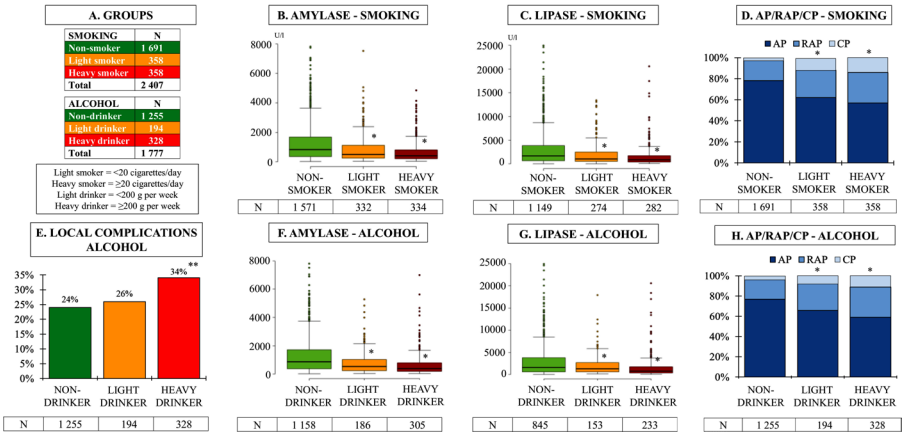

Figure 1 Dose dependency in alcohol consumption and smoking in AP. (A) Light and heavy alcohol consumption and smoking groups and definitions. (B, C) Amylase and lipase levels on admission. (D) Prevalence of RAP and CP (%). (E) Proportion of local complications (%). (F, G) Amylase and lipase levels on admission. (H) Prevalence of RAP and CP (%). *P<0.001, **p=0.003. Pearson's χ^2 test and the Kruskal-Wallis rank sum tests were used. AP, acute pancreatitis; CP, chronic pancreatitis; RAP, recurrent AP.

Second, we examined the possible synergistic effect of these two risk factors. We arranged the cohort population into four groups based on current smoking and alcohol consumption status (figure 2). Smoking and drinking together are associated with the male sex and linked to the first AP episode 15 years earlier than non-smoking and non-drinking are. Analysing on-admission and outcome parameters between groups, we found that amylase and lipase levels are the lowest and the proportion of moderately severe cases are the highest in the smoking–drinking group, suggesting the most pancreatic tissue damage and local complications here. The highest proportion of patients with RAP was found in both smoking groups, and the largest percentage of CP patients was observed in the smoking–drinking population, suggesting a clear synergising effect of alcohol consumption and smoking and a highlighted importance of smoking in progression.

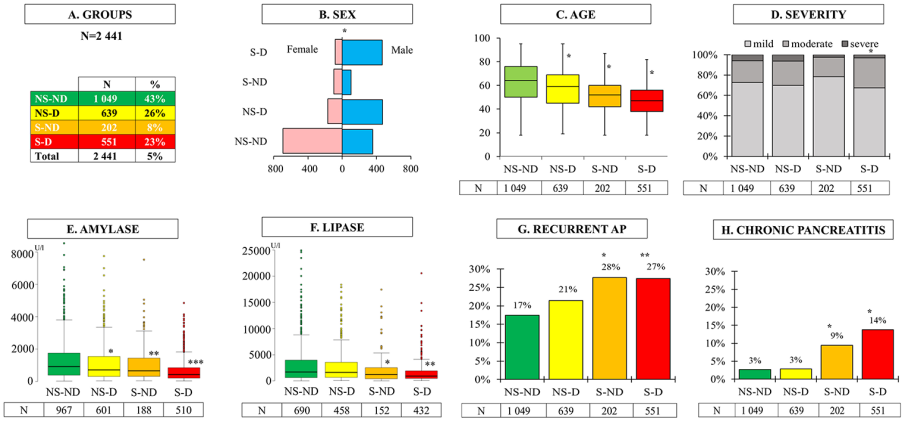

Figure 2 Combined alcohol consumption and smoking groups in AP. (A) Groups. (B) Sex. *P<0.001 in all comparisons. (C) Age. *P<0.001 or p=0.001 in all comparisons. (D) Severity. Moderately severe *p=0.003 vs NS–ND. P=0.022 vs S–ND. (E) On admission amylase level. *P<0.001 vs NS–ND. **P<0.003 vs NS–ND. ***p<0.001 vs NS–ND, NS–D and S–ND. (F) On-admission lipase level. *P<0.003 vs NS–ND, p<0.006 vs NS–D. **P<0.001 vs NS–ND and NS–D. (G) Prevalence of recurrent AP. *P=0.003 vs NS–ND. **p=0.04 vs NS–D. p<0.001 vs NS–ND. (H) Prevalence of chronic pancreatitis. *P<0.001 vs NS–ND, NS–D. Pearson's χ^2 test and the Kruskal-Wallis rank sum tests were used. AP, acute pancreatitis; NS–D: non-smoking–drinking; NS–ND: non-smoking–non-drinking; S–D: smoking–drinking; S-ND: smoking–non-drinking.

Our analysis confirms in a clinical setting that both smoking and alcohol are dose-dependently associated with pancreatic tissue damage and the prevalence of RAP and CP. Moreover, they mutually exacerbate each other's harmful effect. In addition to the development of prognostic and therapeutic measures, further clinical trials on cessation programmes and patient education are needed. Communication to all stakeholders of the importance of at least quitting smoking or cutting the amount of smoking and alcohol consumption is crucial.

Andrea Szentesi,[1,2] Nelli Farkas,[1,3] Zoltán Sipos,[1] Péter Mátrai,[1] Áron Vincze,[4] Ferenc Izbéki,[5] Andrea Párniczky,[1,6] Péter Hegyi ,[1,7,8] Hungarian Pancreatic Study Group

[1]Institute for Translational Medicine, Szentágothai Research Centre, Medical School, University of Pécs, Pécs, Hungary
[2]Centre for Translational Medicine, Department of Medicine, University of Szeged, Szeged, Hungary
[3]Institute of Bioanalysis, Medical School, University of Pécs, Pécs, Hungary
[4]Division of Gastroenterology, First Department of Medicine, Medical School, University of Pécs, Pécs, Hungary
[5]Szent György University Teaching Hospital of Fejér County, Székesfehérvár, Hungary
[6]Heim Pál National Pediatric Institute, Budapest, Hungary
[7]Division of Pancreatic Diseases, Heart and Vascular Center, Semmelweis University, Budapest, Hungary
[8]Centre for Translational Medicine, Semmelweis University, Budapest, Hungary

Correspondence to Professor Péter Hegyi, Division of Pancreatic Diseases, Heart and Vascular Center, Semmelweis University, Budapest, Hungary; hegyi2009@gmail.com

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Collaborators Hungarian Pancreatic Study Group: Bálint Erőss, Péter Jenő Hegyi, Szilárd Váncsa, Rita Nagy, Katalin Márta, Klementina Ocskay, Márk Félix Juhász, Marcell Imrei, Mária Földi, Szabolcs Kiss, Balázs Csaba Németh, Tamás Takács, László Czakó, Szilárd Gódi, Judit Bajor, Patrícia Sarlós, László Gajdán, Mária Papp, József Hamvas, Márta Varga, Melania Macarie, Imola Török, János Novák, Artautas Mickevicius, Elena Ramirez Maldonado, Shamil Galeev, Ville Sallinen, Barnabás Bod, Ali Tüzün Ince, Tamás Nagy, Nándor Faluhelyi, Noémi Gede, Stefania Bunduc, Tamás Hussein, Mónika Lipp, Anna Németh, Orsolya Urbán, Dorottya Tarján, Simon Tóth, Dániel Pécsi, Péter Varjú, Noémi Zádori.

Contributors PH conceptualised the study. ÁV, FI, AS and AP contributed to the data collection and quality assurance. AS, ZS, PM and NF extracted and analysed the data. PH, AS, AP and NF interpreted the data. AS and PH wrote the manuscript. All the authors reviewed and contributed to the manuscript before finalisation and submission. Hungarian Pancreatic Study Group (full names are available in the Contributors section and affiliations are detailed in online supplemental file 1: BE, PJH, SV, RN, KM, KO, FJ, MF, SK, BN, TT, LC, SG, JB, PS, LG, MP, JH, MV, MM, IT, JN, AM, ERM, SG, VS, BB, ATI contributed to the data collection. TN, NF contributed to the interdisciplinary evaluation of the cases. NG conducted preliminary analyses. BE, PJH, SV, RN, KM, KO, FJ, MI, MF, SK, NG, SB, TH, ML, AN, OU, DT, ST, DP, PV and NZ ensured professional data quality control.

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ORCID iD
Péter Hegyi http://orcid.org/0000-0003-0399-7259

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