Tobacco, alcohol and pancreatic disease: key findings from global consortia

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Pancreatic cancer remains the major common cancer site showing unfavourable trends in most areas of the world, including Europe, over the last few decades [1].

There are a few well-recognised risk factors for the disease, which, however, account for a limited proportion of all pancreatic cancers, in general less than a third of all cases.

These include acute – and mostly chronic – pancreatitis, alcohol and tobacco, which – at least in part – may act through an inflammatory process. In other terms, pancreatitis may well be in the mechanistic pathway of alcohol, tobacco and pancreatic cancer.

Clinical evidence indicates that heavy alcohol drinking is consistently related to acute pancreatitis [2, 3]. Epidemiological data are limited, but support a role of (heavy) alcohol drinking, whereas there is no consistent association between moderate drinking and acute pancreatitis. With reference to tobacco in a meta-analysis of five studies of acute pancreatitis, the pooled relative risks (RR) were 1.74 (95% confidence interval, CI, 1.39-2.13) for current and 1.32 (95% CI 1.03-1.71) for former smokers [2, 3].

Chronic pancreatitis is associated to heavy alcohol drinking, though the risk estimates remain open to discussion. Epidemiological data are limited, but consistent with clinical ones to indicate that (heavy) drinking is related to chronic pancreatitis [2]. There is consistent evidence that tobacco is also a major factor for chronic pancreatitis. With reference to tobacco, the RRs from a meta-analysis were 2.8 (95% CI 1.7-4.8) for current and 1.4 (95% CI 1.1-1.9) for former smokers and these associations were not totally accounted for by heavy alcohol drinking [4]. Tobacco is responsible for 10 to 20% of all chronic pancreatitis. In non-alcoholic idiopathic chronic pancreatitis, smoking is associated with disease progression [5].

Cigarette smoking is the major risk factor for pancreatic cancer. In the Pancreatic Cancer Consortium (PanScan; 1481 cases, 1539 controls) the pooled RR was 1.77 (95% CI 1.38-2.26) for current and 1.09 (95% CI 0.91-1.30) for former smokers [6]. In the International Pancreatic Cancer Case-Control Consortium (PanC4; 6507 cases, 12,890 controls), the RR was 2.20 (95% CI 1.71-2.83) for current smokers and rose to 3.39 (95% CI 2.36-1.86) for heavy smokers; the RR was 1.17 (95% CI 1.02-2.83) for former smokers [7]. Cigar smoking was also associated with pancreatic cancer (RR 1.62, 95% CI 1.15-2.29), whereas no consistent association was found for smokeless tobacco, nor for pipe smoking [8]. A meta-analysis of 21 case-control and 11 cohort studies provided conclusive evidence that moderate drinking was unrelated to pancreatic cancer, but heavy drinking (3 or more drinks/day) gave a RR of 1.22 (95% CI 1.12-1.34) [9]. In the PanScan collaborative re-analysis of cohort studies (1530 cases, 1520 controls), there was no overall association with total alcohol intake, but the RR was 1.38 (95% CI 0.9-2.3) for drinking ≥60g day and rose to 2.23 (95% CI 1.0-4.9) for male heavy liquors drinkers [10]. In a pooled analysis of 14 cohort studies (2187 cases) the RR for >30g day was 1.22 (95% CI 1.03-1.45) [11]. In the PanC4 study (5585 cases, 11,822 controls), the RR was 1.46 (95% CI 1.16-1.83) for ≥6 drinks day; no association was observed with moderate drinking [12].

Possible mechanisms of action of alcohol include acetaldehyde, fatty acid ethyl esters, free radicals, DNA damage and inflammation [12]. Possible mechanisms of action of smoking include tobacco specific nitrosamines (NKK), polycyclic aromatic hydrocarbons (PAH) and other smoking-associated chemicals, and smoking as an inflammatory agent and a progressor in carcinogenesis [7].

In conclusions, moderate alcohol drinking is not associated to acute, chronic pancreatitis and pancreatic cancer, but heavy drinking is a major cause of pancreatitis and it is associated to pancreatic cancer. It explains, however, only a small proportion of all cases of pancreatic cancer. Tobacco is consistently associated to acute pancreatitis, chronic pancreatitis, and pancreatic cancer, and it is the major cause of pancreatic cancer, accounting for up to 25% of pancreatic cancer cases on a population level.

Thus, avoiding tobacco smoking remains the key measure to control pancreatic cancer on a global scale. Given the lack of effective screening and early diagnosis instruments, control and reduction of pancreatic cancer mortality in the foreseeable future remains linked to control of tobacco and alcohol excess – plus overweight and diabetes, which also contribute to pancreatic cancer [13].

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