JIM Editorial

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Alcohol-induced pancreatitis and alcohol-related liver disease: Two different phenotypes of alcohol-related harm or related conditions?

It is well known that overconsumption of alcohol can cause tissue injury in the liver and the pancreas, apart from many other organs such as the heart, brain, and peripheral nervous system. It has also been recognized that less than 5% of individuals who drink excessively will develop episodes of acute pancreatitis [1]. The definition of heavy drinking is beyond the scope of this editorial, and obtaining a reliable history of alcohol use can be a challenge. The pattern of use and the lifetime drinking history did not reveal any major differences among patients with alcohol use disorder (AUD) who were hospitalized for alcohol rehabilitation (without a history of alcoholic pancreatitis) and patients previously diagnosed with alcohol-induced pancreatitis (AIP) [2]. In that study, males with AIP had a significantly lower total amount of spirits and a lower proportion of binge drinking than those with AUD, suggesting the *idiosyncratic* etiology of AIP [2]. In a study from Portugal, lifestyle and eating habits seemed to impact the development of alcoholic pancreatitis [3]. Patients with alcoholic liver disease (ALD) had significantly higher alcohol consumption than AIP patients, and the latter group reported a more abundant diet in the past [3]. A Swedish prospective and population-based study revealed that vegetable but not fruit consumption might prevent the development of non-gallstone-related acute pancreatitis [4]. Thus, lifestyle and diet may influence the development of AIP apart from alcohol consumption [2–4]. Although more knowledge is available on the risk of ALD based on threshold values of alcohol consumption, only a minority of heavy drinkers develop ALD [5]. However, the incidence of both ALD and AIP has been shown to increase with increased per capita alcohol consumption in the general population [6].

In the present issue of the Journal of Internal Medicine, Dugic et al. reported a sixfold increase in AIP in patients with ALD compared to matched controls [7]. A total of 7% of the patients had experienced pancreatitis prior to the diagnosis of ALD, suggesting a ninefold higher risk compared with the matched controls. However, the cumulative incidence of hospitalization for AIP in patients with ALP was only 2.7% [7]. Although the risk was higher than in matched controls, the risk seems very low that ALD patients will suffer from AIP. In the study by Dugic et al., independent risk factors for developing AIP were younger age, male sex, and diagnoses of alcohol and obstructive pulmonary disease [7].

The study included an impressive number of patients diagnosed with ALD, and the study has a long follow-up. This was a registry study from good quality health care in Sweden and a socialized medicine system, which means that all patients hospitalized for ALD in Sweden during the study period were included as private hospitals did not have ALD inpatients. Thus, it is a population-based study, which is a big strength without the risk of selection bias. As with other registry-based studies relying on ICD-9 and ICD-10 codes, these are not always reliable. The authors of the current study tried to validate their codes for 200 patients diagnosed with acute pancreatitis, and the positive predictive value was relatively high when accounting for missing data (86%). It was not completely clear if the accuracy of the acute pancreatitis diagnosis reported was only on the presence of AIP or if it also included biliary pancreatitis. The most common cause of acute pancreatitis in Sweden and in other neighbouring countries is biliary or gallstone-induced acute pancreatitis [8]. Thus, as the authors acknowledge, it is likely that some of the patients had biliary pancreatitis. Furthermore, as should be expected from a registry study without scrutinization of medical records, information about the proportion of patients who managed to stop drinking alcohol was not available. Similarly, data on smoking were not available, but the

authors used the diagnosis of chronic obstructive pulmonary disease (COPD) as a marker for smoking. COPD was found to be an independent predictor of the development of acute pancreatitis, which is in-line with previous studies showing that smoking increases the risk of acute and chronic pancreatitis. In the first 20 years of the study period from 1969 to 1989, before the detection of hepatitis C, some of the ALD patients might have suffered from hepatitis C. However, it is unclear how that might have affected the results. In the current study [8], a higher in-hospital mortality was observed in patients with ALD during the incident episode of acute pancreatitis compared to the comparators, 0.3% versus 0.1%. However, this was very low in absolute terms, and although reported as statistically significant, the results were hardly clinically significant.

In summary, the results of the current study are of interest and are probably, despite methodological limitations, the most reliable data published so far on the relationship between ALD and acute pancreatitis. The authors should be congratulated on all their hard work and thorough statistical analysis. However, although there is an increased risk of acute pancreatitis in patients prior to and after the diagnosis of ALD, the risk, particularly after the ALD diagnosis, is very low. Only 2.8% of the ALD patients in the current study developed acute pancreatitis after the established ALD diagnosis. It is conceivable that some patients prone to develop both ALD and AIP might have been more successful in stopping alcohol drinking due to the "antabuse" effect of the usually very painful AIP than ALD patients without prior AIP. It can be concluded that remarkably few patients with ALD also experience pancreatitis due to alcohol and vice versa. The vast majority of patients who will be hospitalized for alcoholic pancreatitis will never develop ALD. It seems that these two phenotypes, ALD and AIP, have very different genetic risks [9, 10].

Conflict of interest statement

The author declares no conflicts of interest.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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