RESEARCH LETTER

Intense and Sustained Alcohol Consumption Associated With Acute Pancreatitis Warrants Early Intervention

Acute pancreatitis (AP) is a leading cause of gastrointestinal disease-related hospitalizations in the United States, with 1%–2% mortality per episode.[1,2] Repeated AP episodes lead to chronic pancreatitis (CP) and poor quality of life.[3] Alcohol use is one of the most prevalent causes of AP, and continued drinking can trigger recurrent attacks of AP.[3] We previously found heavy and sustained drinking in CP patients prior to diagnosis, amounting to >30,000 drinks over a lifetime.[4] We sought to examine the extent of drinking and comorbid conditions in AP and recurrent AP (RAP) patients to inform intervention strategies.

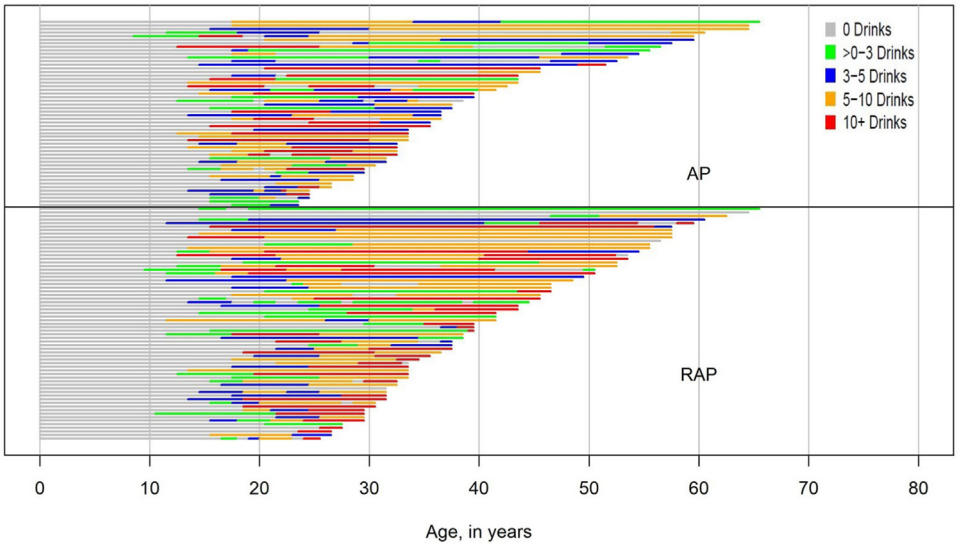
A Case-CrossovEr study deSign to inform tailored interventions to prevent disease progression in AP (ACCESS-AP, NCT04743323) is an ongoing observational, multicenter study[5] to examine drinking patterns and associated health behaviors in hospitalized AP or RAP patients who demonstrate moderate to heavy drinking as defined as Alcohol Use Disorders Identification Test Consumption (AUDIT-C) score of ≥3. Detailed description of the study and subject eligibility is available in the Supplementary Material and the published protocol.[5] Patients with CP (defined by the presence of pancreatic calcifications on cross-sectional imaging) were excluded. Briefly, drinking history was assessed using a modified version of Skinner and Sheu's questionnaire for lifetime drinking history.[6] As of December 2022, we enrolled 128 patients with an AP episode, of whom subjects (n = 117) with complete lifetime drinking data were included in the current analysis; 52 were enrolled at their first AP episode and 65 had prior history of ≥1 attacks of AP. The median age of enrollment was 38 years, and the majority of patients identified as male (67.5%), White (52.1%), and non-Hispanic or Latino (82.1%). Two-thirds (67%) of patients reported ever smoking cigarettes.

Our cohort began drinking at moderate levels <5 drinks/day at a median age of 16–17 years, with increasing intensity over time (Figure). At their peak drinking phase, AP and RAP patients drank 7 and 10 drinks per drinking day and drank at this intensity for a median duration of 20.5 and 20 years, respectively. At enrollment, 23.1% of AP and 41.5% of RAP patients drank ≥6 drinks per occasion on a daily basis in the past year. Additionally, 25.0% of AP and 16.9% of RAP patients drank ≥6 drinks per occasion on a weekly basis. Over a lifetime, AP patients consumed a median of 17,076 drinks, and RAP patients consumed 32,491 drinks ($P = .013$). As a frame of reference, alcohol-associated CP patients in North America consumed 7 drinks per drinking day during their peak phase, reaching lifetime consumption of 34,388 drinks over a longer duration of 28 years.[4] Given the similarity in drinking levels between RAP and alcoholic CP patients,[4] it is likely that RAP patients will progress to CP unless drinking discontinues.

Intervention starts with recognition of the alcohol use disorder, which was diagnosed in 25% and 40% of the AP and RAP patients in our study. Among AP and RAP patients with a diagnosis of substance use disorder, the median AUDIT-C score was higher than those without this diagnosis (10 vs 8). Notably, an AUDIT-C score of ≥8 indicates harmful and hazardous drinking according to the National Institute of Alcohol Abuse and Alcoholism.[7] Despite heavy drinking, 31% of AP and 49% of RAP patients noted having undergone detoxification treatment, and 23% and 31% were in inpatient settings, respectively (Figure, Table A1).

After enrollment, AP and RAP patients experienced a high rate of independent episodes of RAP (28% vs 49%) over a short median follow-up period of 8 months (Figure and Figure A1). Two prior studies of alcohol-associated AP patients reported 30-day readmission rates of 12% and 70%, respectively, with more than half of the readmissions being related to alcohol.[8,9] Furthermore, other studies showed recurrence rates of AP of 43.1% in 11 months, 21% in 2 years, and 65% in up to 13 years of follow-up.[10–12] Collectively, this demonstrates higher recurrence rates in alcohol-associated AP than in AP patients with non-alcoholic etiologies (10%–30%).[3] Alcohol cessation intervention after the first AP episode may help to mitigate a pattern of high alcohol intake and recurrent attacks.[13,14] Although it is common practice to provide brief alcohol intervention during hospitalization, prior research highlights the need for better approaches.[11] A randomized controlled trial demonstrated that scheduling visits every 6 months for repeated counseling against alcohol consumption was more effective in reducing the risk of developing RAP than when a single standardized alcohol intervention during hospitalization. The intervention comprised a 30-minute conversation covering: (1) the harmful effect of alcohol on the pancreas, (2) the need to change one's drinking habits and one's responsibility toward change, and (3) the social problems encountered so they could be addressed.[11] Overall, such interventions can reduce alcohol use, hospitalizations for repeated attacks, and the risk of developing CP.[11]

Concomitant mental health conditions were prevalent in our patients including depression (40.2%) and anxiety (45.3%) (Table A1). Among patients who reported being diagnosed with any mental health condition, 49.6% received care from a mental health specialist. Negative life events related to family (52%), death (52%), residence (33%), financial matters (41%), and jail (31%) were frequently



Measure	AP (n=52)	RAP (n=65)	Total (n=117)	P-Value
# of drinks per day during maximum drinking period Median [IQR]	7 (5 – 12.2)	10 (7 - 16)	9 (5 - 15)	0.126
Average # of drinks per day during periods of drinking Median [IQR]	4.8 (3.4 – 7.7)	6 (4.4 - 9.4)	5.5 (3.9 – 9.2)	0.085
Cumulative lifetime alcohol consumption, number of drinks Median [IQR]	17076 (10219.5 - 44958)	32491.5 (17280 - 59184)	24720 (12720 - 51552)	0.013
AUDIT-C Score Summary Median [IQR]	8 (6-10)	9 (7-11.5)	9 (7-11)	0.086
Underwent alcohol detoxification treatment (Inpatient OR Outpatient)	16 (30.8%)	32 (49.2%)	48 (41%)	0.044
[a]Recurrent AP in follow up	12 (27.9%)	20 (48.8%)	32 (38.1%)	0.049

Figure. Individual alcohol consumption patterns of acute pancreatitis (AP) and recurrent acute pancreatitis (RAP) patients. Individual bars on the heat map represent the duration of participant-specific self-reported drinking by phases while the colors of each bar represent the number of drinks consumed on drinking days by phases. [a]The final analytic sample size for those who completed at least 6 months of follow up is 84.

reported in association with the peak drinking phase. Studies on integrated treatment in which the clinician or treatment team simultaneously manages the patient's mental disorder and alcohol use disorder suggest that integrated treatment yields positive outcomes.[15]

The current study has some limitations. Firstly, some AP patients may have had CP if they did not have a calcified form of CP. However, all patients included in our study met the Revised Atlanta Classification of AP and were experiencing acute onset pain. Secondly, although a validated instrument was used to assess lifetime drinking, patients may not accurately remember all details about their past drinking behaviors, potentially leading to misclassification and underestimation of drinking. In fact, the extent of drinking may be greater than reported. Lastly, we did not study controls with alcohol consumption of similar intensity. Future studies that incorporate behavior controls would be valuable in further elucidating the relationship between alcohol consumption and AP and comorbid conditions unique to AP.

In summary, the higher lifetime cumulative drinking and heavy daily alcohol use in RAP vs AP patients suggest disease progression toward CP. Moreover, these patients have a high burden of mental health conditions are potentially influenced by adverse life circumstances. Our data support the need for developing an integrated treatment program, which addresses alcohol cessation after the first AP episode. This program should also include behavioral interventions to address concomitant mental health and psychosocial problems to reduce the risk of recidivism and recurrence of pancreatitis. Intervening early in alcohol-associated AP could prevent further progression to RAP and mitigate the risk of CP.

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Supplementary materials

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Abbreviations used in this paper: **AP, acute pancreatitis; AUDIT-C, Alcohol Use Disorders Identification Test Consumption; CP, chronic pancreatitis; RAP, recurrent acute pancreatitis**

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Ethical Statement:
The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

Data Transparency Statement:
Data available on request after the completion of the study aims.

Reporting Guidelines:
STROBE.