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Recent Advances in the Epidemiology of Alcoholic Pancreatitis

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Abstract Clinical observation has defined the medical profile of alcoholic pancreatitis, but its low incidence and prevalence has limited characterizing the disease at a population level, the contribution of environmental exposures, and a clear picture of its natural history. Recent studies have defined the impact of alcohol use and smoking on disease risk, and a threshold for alcohol consumption has been identified. Recurrent attacks of acute pancreatitis have been linked with continued alcohol consumption, and aggressive alcohol intervention has been shown to decrease recurrence. Progression from alcoholic acute pancreatitis to chronic pancreatitis is now believed to occur infrequently, and factors associated with progression have been identified. Alcoholic pancreatitis reduces lifespan in these patients, and the economic impact of pancreatitis is substantial. Efforts are needed to increase awareness of the impact of alcohol consumption and smoking on risk for pancreatitis and the benefits of cessation for primary and secondary prevention.

Keywords Alcohol · Pancreatitis · Epidemiology · Smoking · Incidence · Prevalence · Natural history · Recent advances · Recurrences · Prevention

Introduction

A major change has occurred in our understanding of the link between alcohol and pancreatitis over the past decade. Initial observations from the 1960s to the 1990s, mainly from specialized centers, clarified the clinical profile and natural history of alcoholic chronic pancreatitis (CP) [1–8]. Recent studies have used a population-based or multicenter approach to address many unanswered questions and provide a new perspective on the epidemiology of alcoholic pancreatitis. These reports have described the distribution of pancreatitis at a population level and its economic impact, and have better defined the relationship between environmental exposure with risk, recurrence, progression, and survival. This review focuses on findings of recent epidemiologic studies and how they fill gaps in our understanding of pancreatitis.

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Definition of Alcoholic Pancreatitis

No universally accepted criteria exist to assign alcohol as an etiology of a patient's pancreatitis. Experts have used definitions varying from consumption of over 50 to 80 g (ie, 4 to 7 drinks/day) with or without a minimum drinking duration [3, 6, 9, 10]. An international consensus panel defined alcoholic CP based on typical clinical history, threshold alcohol consumption (80 g or more of alcohol for a few years in males, less in females), and morphological evidence of CP on imaging studies or histology [11].

Alcohol as an Etiology for Pancreatitis

Alcohol is the second most common cause of acute pancreatitis (AP) after gallstones, and the most common cause for CP [12]. Table 1 outlines the proportion of patients with alcoholic CP in population-based and non–population-based studies [3, 4, 6–8, 10, 13, 14•, 15, 16•, 17,

Table 1 Alcohol as the etiology of chronic pancreatitis in selected studies

Study, publication year	Country	Study period	Population studied/ Number of centers	Number of patients	Males, %	Alcohol etiology, %
Population based						
Lin et al. [17], 2000	Japan	1994	Nationwide	2523	78	55
Dite et al. [15], 2001	Czech Republic	1999	Czech Republic	52	62	60
Lankisch et al. [10], 2002	Germany	1988–1995	Luneberg	74	78	72
Nojgaard et al. [18•], 2010	Denmark	1977–1982	Copenhagen	290[a]	72	44[b]
Non-population based						
Marks et al. [7], 1973	South Africa	1960–1972	Single	734	~ 80[c]	80
Ammann et al. [13], 1987	Switzerland	1953–1986	Single	287	88	71
Dani et al. [4], 1990	Brazil	1963–1987	Two	797	91	90
Robles-Diaz et al. [8], 1990	Mexico	1977–1982	Single	150	80	68
Layer et al. [6], 1993	United States	1976–1982	Single	448	65	56
Cavallini et al. [3], 1997	Italy	1971–1995	Single	715	88	79
Frulloni et al. [16•], 2009	Italy	2000–2005	Multicenter	893	74	43
Cote et al. [14•], 2010	United States	2000–2006	Multicenter	540	52	45

[a] Includes definite and probable chronic pancreatitis

[b] Alcohol consumption>50 g/d was reported by 57% of patients

[c] Exact number not provided

18•]. In observational studies from the 1960s to the 1990s, alcohol was cited as the predominant etiology of CP (60%–90%). It is noteworthy that although alcohol continues to be the dominant etiology, the proportion of patients in whom alcohol is attributed as a single or contributing etiologic factor has been lower in recent multicenter studies (~ 50%).

In the United States, two large studies have reported on alcohol consumption in CP patients. Among 448 CP patients evaluated at the Mayo Clinic from 1976 to 1982, Layer et al. [6] found that 18% were lifetime abstainers, 18% consumed moderate amounts of alcohol (< 50 g/d), and 56% were heavy drinkers (> 50 g/d), whereas alcohol consumption was unknown in nearly 8% patients. Patients who consumed more than 50 g/d were considered to have alcoholic etiology [6]. A recent multicenter US study prospectively enrolled 540 CP patients from 2000 to 2006 from 19 centers with specific interest in pancreatic diseases. Physicians considered alcohol as the sole or contributing cause of CP in about 45% patients [14•]. The proportion of CP patients diagnosed with alcohol etiology was higher (79%) in an earlier single center Italian study (715 patients evaluated from 1971 to 1995) [3] compared with a recent multicenter study of 893 patients enrolled from 2000 to 2005 (alcohol etiology, 43%) [16•].

Regarding these studies, three potential factors need consideration. First, both recent multicenter studies have drawn patients from referral centers. The spectrum of disease at a population level may be quite different from those evaluated at specialized centers: it is likely that patients referred to specialized centers include those for whom no specific etiology for CP could be determined or who have more symptomatic or complicated disease. Second, cross-sectional imaging (CT and MRI) has become highly sensitive to detect morphological changes in the pancreas, thereby leading to earlier diagnosis. Third, the proportion of females in the patient cohort would affect the overall proportion of patients with alcohol etiology; the lower prevalence of alcohol etiology in the US studies compared with the European centers could be due in part to a higher proportion of females.

Whereas the peak age for presentation of alcoholic pancreatitis is uniformly 40 to 60 years, incidence differs based on sex, race, and geographic distribution [12]. Patients with alcoholic pancreatitis are more likely to be male (70%–75%). Lankisch et al. [19] determined that at equal levels of consumption, the rates of alcoholic pancreatitis are similar for both sexes. Thus, overrepresentation of males among patients with alcoholic pancreatitis reflects a higher prevalence of alcohol consumption than sex-based differences in susceptibility. Compared with whites, the rates of alcoholic pancreatitis are two- to threefold higher among blacks [20]. This observation, initially reported by Lowenfels et al. [20], has been confirmed by several investigators [21, 22•, 23]. However, the reasons for racial differences in susceptibility to pancreatitis are unclear and need further study. The incidence of alcoholic pancreatitis varies among countries and regions, likely because of differences in the alcohol consumption or distribution of other known or unknown cofactors that accompany alcohol consumption.

Economic Burden of Pancreatitis

The economic impact of pancreatitis is substantial. A recent US study used data from a variety of government sources to determine the inpatient, outpatient, and long-term care costs for digestive disorders [24]. The total estimated costs of pancreatitis for non-federal institutions and physicians in 2004 were $3.7 billion. The number of hospital admissions and ambulatory visits in which pancreatitis was the first-listed diagnosis were 277,000 and 475,000, respectively. Among all digestive disorders, pancreatitis ranked eighth in overall health care costs to society and seventh in hospital admissions and charges.

Another study using the National Inpatient Sample estimated the number of hospital discharges from non-federal US hospitals with a primary diagnosis of AP in 2003 to be 225,600 and the direct medical costs associated with these to be $2.2 billion [25]. On univariate analyses, the determinants of costs were increasing age, length of stay, urban (vs rural) hospitals, teaching (vs nonteaching) hospitals, and geographic region. In multivariable models, the significant predictors were length of stay and regional differences (higher in Western US vs South).

These studies did not stratify cases by etiology. Assuming that alcohol accounts for about 25% to 30% of all cases of AP and 50% of all cases of CP, about 40% of these costs are likely to be alcohol-related. Another limitation of the above studies is that they analyzed information on individual episodes (ie, admissions) or service provided (ie, ambulatory visits) rather than unique patients. Thus, the estimated costs only reflect aggregate information, and it is difficult to know whether the resource utilization is uniformly distributed or skewed by a small fraction of patients. Nonetheless, these estimates provide valuable information to generate new hypotheses and conduct detailed analyses to identify high-risk patients who may benefit from focused approaches to improve outcome and reduce health care costs.

Natural History of Alcoholic CP

Although a population-based approach in unselected patients is the best way to understand the distribution and natural course of a disease, most natural history studies in CP are based on data from single or multicenter experiences and have compared the clinical course of alcoholic with idiopathic CP in general or after stratification into early- or late-onset disease (ie, symptom onset before or after 35 years of age) [5, 6, 13, 26].

The clinical features at the time of initial presentation in alcoholic CP are shown in Fig. 1a. About 75% of patients present with either an attack of AP (~ 50%–55%) or abdominal pain (20%–25%), whereas the remaining patients present with jaundice from distal common bile duct obstruction, exocrine or endocrine insufficiency, or an incidental diagnosis. Overall, about 90% of patients have pain, 50% develop exocrine and/or endocrine insufficiency, and 30% to 35% require pancreatic surgery during their clinical course. In general, the probability of achieving pain relief increases over time, which may or may not coincide with development of other features of "burnout" of the pancreas (eg, calcifications, exocrine or endocrine insufficiency) [6, 13, 26]. Overall survival in patients with alcoholic pancreatitis is significantly lower compared with the background population, and most patients die from causes unrelated to pancreatitis [18•, 27].

The natural history of alcoholic CP is distinctly different from idiopathic CP, especially the late-onset type. Patients with alcoholic etiology have more symptomatic disease characterized by a higher frequency of pain, attacks of acute or recurrent AP, or complications (eg, pseudocysts).

Alcohol and the Risk of Pancreatitis

The prevalence of changes attributable to CP in autopsies of alcoholic individuals is much higher than those observed in clinical studies, suggesting that subclinical damage to the pancreas is more common in alcoholic subjects than is reported. A recent study assessed histology in 7541 subjects—of whom 620 (8%) had a diagnosis of alcoholism—and showed a prevalence of CP changes of 13.7% [28•]. Unfortunately, the investigators did not have information on what fraction of patients had clinically diagnosed disease. In the same study, the prevalence of cirrhosis among alcoholics was 30%. A high degree of overlap was seen, with 18% of patients with cirrhosis also demonstrating CP changes, and, conversely, 38% patients with CP showing cirrhotic changes of the liver. Such concurrent damage in alcoholic subjects suggests that at least some factors and/or mechanisms for organ damage are similar across organs.

In a study of male veterans, the prevalence of existing diagnosis codes was used as a surrogate for lifetime risk of clinical pancreatitis [29]. The prevalence of any pancreatitis, AP, and CP codes was 0.98%, 0.76%, and 0.4%, respectively, among veterans who did not have associated diagnosis codes for alcoholism; the prevalence was about fivefold higher among veterans who also had an alcoholism diagnosis (any 5.9%, acute 4.7%, chronic 3%).

Kristiansen et al. [30•] evaluated the probability of receiving a pancreatitis diagnosis in a cohort of about 18,000 men and women followed for a mean of 20 years. The risk of any pancreatitis among self-reported abstainers at the time of initial evaluation was 1.33% (0.89% AP, 0.4% CP) and among individuals who consumed 35 or

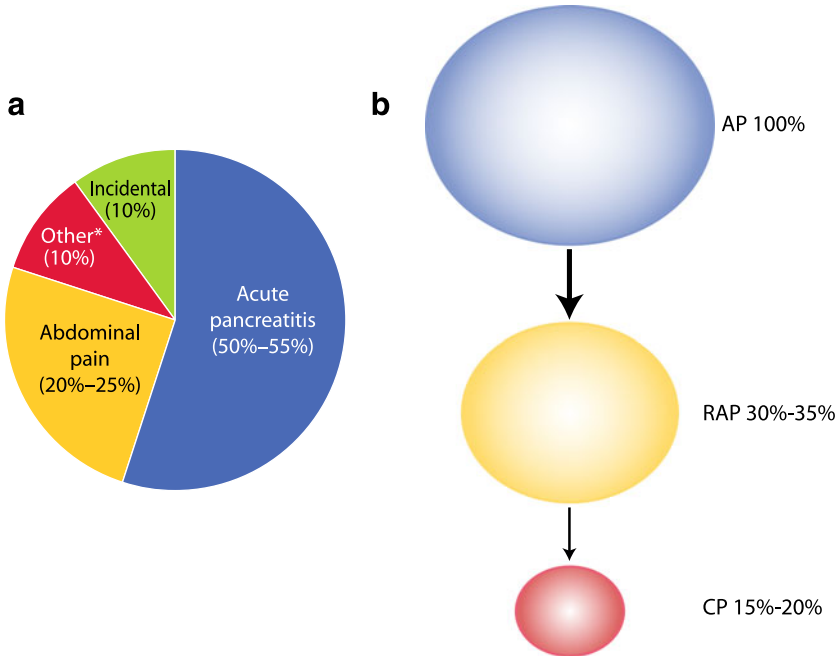

Fig. 1 **a** Clinical symptoms at the time of initial presentation of alcoholic chronic pancreatitis. Other symptoms (*) include exocrine insufficiency, diabetes, jaundice, and weight loss. **b** Natural course of progression from alcoholic acute to chronic pancreatitis. Recurrent attacks (RAP) of acute pancreatitis (AP) occur in about one in every three patients, and chronic pancreatitis (CP) develops in about one in five patients with alcoholic acute pancreatitis

more drinks/week (5 or more drinks/day) was 2.5% (1.6% acute, 1.3% chronic). Lowenfels et al. [27] have also estimated the risk of pancreatitis among heavy drinkers (5 or more drinks/day) to be about 2% to 3%.

When Kristiansen et al. [30•] evaluated data at individual drinking levels up to 5 drinks/day, the hazard ratios are linear but in the range of 1.5, beyond which the hazard ratio rises to 3 or more with the consumption of 5 or more drinks/day. In another multicenter study of prospectively ascertained CP patients (n=540) and controls (n=695), the odds ratios associated with a drinking level of 5 or more drinks/day were similar (OR 3.1), but no linear relationship was observed. Similarly, Irving et al. [31•] performed a meta-analysis of existing data and confirmed that rather than a linear relationship, there is a threshold of alcohol consumption that increases the risk of pancreatitis significantly (4 drinks/day).

The Danish study also evaluated whether the type of beverage (beer, wine, spirits) or the frequency of drinking (monthly, weekly, almost daily, or daily) is associated with the risk of pancreatitis [30•]. These investigators found an association with beer consumption (> 14 per week) but not with wine or spirits. However, the data were limited by few cases at higher levels of consumption for these beverages. Moreover, the effect of consuming more than one beverage type was not evaluated. After controlling for the amount of alcohol consumption, the investigators did not find an association with frequency of consumption.

Overall, risk of pancreatitis increases only with higher alcohol exposure than is seen with other diseases. For example, the estimated threshold for increased risk is about 2 drinks/day for heart and chronic liver disease.

Drinking behaviors can vary widely over an individual's lifetime [32]. Data are sparse on the effect of cumulative alcohol consumption, drinking pattern, or drinking trajectory across the lifespan on pancreatitis. This is specifically important, given increasing evidence that susceptibility to several diseases may also be linked to drinking pattern and trajectory [33, 34]. Data from studies of patterns and trajectories may provide important clues regarding individual susceptibility to pancreatitis, the relationship of specific symptoms of pancreatitis (abdominal pain, AP, pancreatic endocrine/exocrine insufficiency), disease progression (from AP to CP), and development of complications.

Relationship Between Smoking and Alcoholic Pancreatitis

The prevalence of pancreatitis in all populations indicates that susceptibility due to alcohol is not limited by sex, race, or geographic location, but likely has other environmental and/or genetic cofactors. The environmental factor that has gained the most attention as a potential contributor to CP risk is smoking. Since the first report linking smoking and CP about 30 years ago [35], several epidemiology studies (selected studies are outlined in Table 2) using different study designs have firmly established smoking as a risk factor for pancreatitis [21, 22•, 36–39, 40•], and a meta-analysis on the relationship between smoking and CP was recently published [41•].

In a recent cohort study from Sweden [42], smoking was noted to be a dose-dependent risk factor for AP after

Table 2 Association between smoking and chronic pancreatitis in selected studies

Study, country, publication year	Study design	Control group	Gender	Measure of association	Group	Strength of association for group[a]
Yen et al. [35] (USA) 1982	Case-control	Hospital patients	Both	OR	Males:	
					Ex-smoker	4.6 (1.1–19.1)
					Current smoker, < 1 PPD	10.2 (2.2–45.8)
					Current smoker, > 1 PPD	13.4 (3.3–53.8)
					Females:	
					Ex-smoker	1.9 (0.8–4.4)
					Current smoker, < 1 PPD	2.4 (0.8–7.1)
					Current smoker, > 1 PPD	2.3 (1.0–5.6)
Lowenfels et al. [38] (USA) 1987	Case-control	Cirrhosis	Both	OR	Ever smoker	12.5 (1.9–82)
Bourliere et al. [36] (France) 1991	Case-control	Outpatients	Males	RR	–	Each g/d—1.01
Talamini et al. [39] (Italy) 1996	Case-control	Outpatients[b]	Males	OR	< 10 g/d	8.91 (4.5–18.2)
					11–20 g/d	14.3 (8.2–25.2)
					> 20 g/d	12.5 (6.7–23.3)
Lin et al. [37] (Japan) 2000	Case-control	Hospital patients	Males	OR	Current smoker	7.8 (2.2–27.3)
Mortan et al. [21] (USA) 2004	Cohort	Health plan members	Both	RR	< 1 PPD:	
					Alcohol pancreatitis	2.7 (1.5–4.9)
					Idiopathic pancreatitis	1.9 (1.1–3.3)
					> 1 PPD:	
					Alcohol pancreatitis	4.9 (2.2–11.2)
					Idiopathic pancreatitis	3.1 (1.4–7.2)
Tolstrup et al. [40•] (Denmark) 2009	Cohort	Population	Both	HR	Former smoker	1.7 (1.0–2.7)
					1–14 g/d	1.5 (0.9–2.5)
					15–24 g/d	2.5 (1.5–3.9)
					≥ 25 g/d	3.3 (1.9–5.8)
Yadav et al. [22•] (USA) 2009	Case-control	Spouses, family members, unrelated	Both	OR	< 12 pack-years	1.34 (0.9–2.01)
					12–35 pack-years	2.15 (1.46–3.17)
					> 35 pack-years	4.59 (2.91–7.25)

[a] Comparison group—never smokers

[b] All subjects had alcohol consumption>40 g/d

HR hazard ratio, *OR* odds ratio, *PPD* packs per day, *RR* relative risk. One cigarette has 1 gram of tobacco; one pack has 20 cigarettes

controlling for age, sex, body mass index, and alcohol consumption. Two other recent studies—one population-based based cohort study from Denmark [40•] and another case-control study from the United States [22•]—evaluated the association between smoking and CP after controlling for similar confounders. In both studies, smoking was observed to have a dose-dependent association with CP. Heavy smoking increases the risk of pancreatitis by about three- to fourfold compared with nonsmokers, and the magnitude of its association is similar to alcohol consumption. The possibility of an interactive relationship between smoking and alcohol was also evaluated. Although no definitive statistical association could be demonstrated (which may be the result of sample size issues or a high correlation between smoking and alcohol consumption), a careful evaluation of the associations indicates that the magnitude of the effect of smoking is likely multiplicative with increasing levels of alcohol consumption [22•].

Lankisch et al. [43•] noted that smoking increases the risk of progression from AP to CP by about fourfold. Maisonneuve et al. [44] used age of disease onset, development of calcifications, and pancreatic dysfunction (diabetes) as surrogate markers to assess the role of smoking in disease progression. When compared with nonsmokers, patients with alcoholic CP who were smokers were about 5 years younger at the time of diagnosis, and had a fivefold risk of developing calcification and a twofold increase in the risk of developing diabetes during the course of their disease. Talamini et al. [45] used a similar approach to evaluate the role of smoking cessation after diagnosis on

disease progression: the risk of developing calcifications in subjects who stopped smoking after diagnosis returned to baseline (ie, similar to nonsmokers), whereas the risk was increased about twofold in patients who continued smoking after diagnosis.

These reports provide a strong rationale for physicians to routinely counsel patients with AP and CP about the effects of smoking and to facilitate their enrollment into cessation programs if needed. Future studies should focus on documenting how often pancreatitis patients are counseled to stop smoking, how often patients seek or complete formal smoking cessation programs, measures to improve compliance, and the impact of smoking cessation on CP symptoms.

Recurrence After AP and Progression of AP to CP

Although abdominal pain and AP are the most common presenting symptoms of CP, whether and how often AP progresses to CP and the factors associated with such progression has been a matter of debate. In the revised Marseille classification of pancreatitis [46], it was concluded that progression from AP to CP is extremely uncommon and that, although alcoholic CP may present with a clinical episode of AP, most patients already have coexistent CP by the time of presentation with the first episode of AP.

The progression of recurrent alcohol-related AP to CP has been evaluated by Ammann et al. [2, 9]. In a prospective series of 140 patients with alcoholic recurrent AP followed for an average of 16 years (median duration from onset of AP, 13 years), progression to CP occurred in 109 (78%) cases [2]. Among the 109 patients who developed CP, none had coexistent CP at the time of AP diagnosis, but was confirmed during follow-up in about 20%, 50%, and 95% of patients at 2, 6, and 12 years after AP diagnosis. In a subsequent report, the authors evaluated factors that predict disease progression in a larger cohort of patients [9]. They stratified 254 patients with alcoholic CP into those with progressive CP (calcific, 73%; noncalcific, 12%) and nonprogressive CP (or only recurrent AP, 13%). The number of attacks of AP (total and severe) was higher in patients with progressive CP compared with those who only had recurrent AP. Although the overall prevalence of pseudocysts was similar in the two groups (~ 40%), they occurred more frequently in the head of the pancreas in the progressive group. Histology available in seven patients with recurrent AP demonstrated significant fibrosis in four patients, but the exocrine and endocrine functions were preserved in all patients. The authors concluded that their findings are consistent with the "necrosis-fibrosis" theory [47], which proposes that progression to CP occurs as a result of fibrosis in areas of necrosis, and that fibrosis in the pancreatic head causes obstruction of the pancreatic ducts, leading to destruction of upstream acinar tissue.

Pelli et al. [48] retrospectively evaluated the frequency of recurrence in 562 patients admitted with their first attack of alcoholic AP from 1972 to 1992. AP recurred in 260 of these patients: once in 51% of patients; twice in 19%; three times in 15%; and four or more times in 15%. Most recurrences (80%) occurred within the first 4 years following the first attack of AP. The features associated with recurrence were age less than 45 years and mild severity of the initial attack; because of the retrospective study design, the role of continued alcohol consumption or smoking could not be evaluated. In a follow-up study by the same group, 68 patients with a first attack of alcoholic AP were prospectively followed for a median of 38 months (range 25–61 months) [49]. Alcohol consumption and smoking exposure in the months preceding the attack and the 2 years after were assessed. Pancreatitis recurred in 17 patients (25%). The factors associated with recurrence included the use of sedatives prior to initial attack (indicating problems with addiction) and a tendency for higher alcohol consumption, as indicated by higher scores on standardized questionnaires. Total abstinence from alcohol after initial diagnosis was reported by 19% patients, and none of them had a recurrence during the follow-up period. Interestingly, severity of the initial attack was not associated with recurrence. The authors did not find any association between smoking and recurrence, which could be related to an overall low prevalence of smokers in their cohort (60%), a small sample size, and limited duration of follow-up.

Lankisch et al. [43•] evaluated the natural history in 532 residents of Luneberg County, Germany, who had their first episode of AP due to any cause from 1987 to 2004. The etiology of AP was alcohol abuse in 30%, gallstones in 42%, idiopathic in 20%, and other causes in 8% of patients. Patients had a 17% probability of developing one or more recurrences at any time during an average follow-up period of 7.8 years. The risk of recurrence was higher in patients younger than 40, in males, and in those with alcohol etiology (33% compared with 12% in biliary and 5% in idiopathic). Overall, only 4% patients progressed to CP, and all of these patients had alcohol etiology. The cumulative risk of developing CP in patients with alcohol-related AP was about 15% at 10 years; in patients who had a second episode of AP, risk increased to 38% at 2 years and to 42% at 10 years. The study does not indicate whether any patient had coexistent CP at the time of first attack of AP or shortly thereafter. Patients who reported heavy smoking (> 30 cigarettes/day) were 4.3 times more likely to progress to CP after controlling for demographic factors and alcohol consumption. Interestingly, discontinuation of alcohol consumption and smoking did not influence disease progression.

The overall risk of recurrence in AP of these German patients was similar (20%), but progression to CP (15%) was higher in a study from Japan [50•]. Using a nationwide registry of 2533 patients who suffered their initial attack of AP in 1987, Takeyama [50•] conducted a follow-up evaluation in a subset of patients (n=714, 28%) in 2000. The methodology for follow-up (ie, survey vs review of records) was not specified. The etiology of AP was alcohol in 39%, gallstones in 17%, idiopathic in 23%, and other etiologies in 21% of patients. The severity of AP was moderate in 44% and severe in 56% of patients. The risk of recurrence, progression to CP, and development of diabetes was significantly higher in alcoholic AP (32%, 26%, and 21%, respectively) when compared with other etiologies. The relationship of these outcomes with alcohol consumption during follow-up was also evaluated in a subset of patients (n=450). About one third of patients discontinued alcohol consumption completely, and an equal proportion reduced or maintained consumption at previous levels. The probability of recurrence (58% vs 20%), progression to CP (41% vs 14%), and development of diabetes (37% vs 14%) was significantly higher in patients who maintained prior drinking levels. Interestingly, the risk of recurrence, transition to CP (5.1% vs 16.2%), and development of diabetes (7.1% vs 14.4%) in patients with pancreatic necrosis were similar compared with those without necrosis.

Thus, alcoholic AP does transition to CP in about one in five patients (Fig. 1a) and is more likely to occur among subjects with recurrent attacks and who continue their alcohol consumption and smoking. Transition from AP to CP for etiologies other than alcohol is less common, and more studies are needed to better understand these differences. A lack of correlation between pancreatic necrosis during initial AP attack with subsequent development of CP suggests that patients with the classic "necrosis-fibrosis" sequence, as described by Ammann et al. [9], represent a subgroup of patients with alcoholic pancreatitis who have more aggressive disease and clinical course.

Preventing Recurrence of Alcoholic Pancreatitis

In the absence of targeted therapies, treatment of alcoholic pancreatitis is supportive. Although physicians usually counsel patients to abstain from drinking, they are often skeptical whether patients follow their advice. Systematically collected data are few on how often counseling is offered to patients with alcoholic pancreatitis, how often patients comply with such a recommendation, and what might contribute to poor compliance.

Nordback et al. [51•] conducted a carefully designed randomized controlled trial to determine whether alcohol intervention after the first attack of alcoholic AP could reduce recurrence. The primary outcome measure was frequency of recurrent attacks of AP during a minimum follow-up of 2 years. The investigators randomly assigned 120 patients admitted with their first attack of pancreatitis into either a control (n=61) or treatment arm (n=59). Control subjects received a 30-minute counseling session by a trained nurse during hospitalization that focused on how alcohol affects the pancreas, the social effects of alcohol consumption, the fact that no amount of alcohol may be safe, and the need for the patient to take personal responsibility to stop drinking or seek additional services if needed. In addition to the initial counseling while hospitalized, patients in the intervention group received additional counseling sessions every 6 months. A significant reduction was observed in the number of patients who developed recurrence (21% vs 8%, P=0.042), the number of recurrent episodes (20 vs 9, P=0.012), number of days of hospital admission (120 vs 44 days), and the number of hospital admissions for abdominal symptoms (30 vs 15, P=0.004). The impact of alcohol intervention was apparent only after 6 months of follow-up, indicating that repeated intervention was the key to the observed outcomes. The authors determined that alcohol intervention in about 7.5 patients would be needed to prevent one recurrence. They also noted that patients who refused to enroll in the trial were at the highest risk for recurrence (28%) and that four out of 39 (15%) patients who did not participate developed CP during follow-up.

The results of this study provide strong empiric evidence that the natural history of alcoholic pancreatitis can be altered by aggressive counseling with periodic follow-up and reinforcement. Although not directly studied, these results also provide a strong rationale that such an intervention could reduce the risk of progression from alcoholic AP to CP. This strategy will be ideal in the primary care setting, where patients are more likely to be followed longitudinally. Therefore, educating gastroenterologists as well as primary care physicians on the benefits of aggressive risk-factor management in patients with alcoholic pancreatitis should be a priority.

Conclusions

Recent studies have improved our understanding of the epidemiology of alcoholic pancreatitis in several ways. The risk of pancreatitis with alcohol consumption is better defined, and a threshold level of consumption associated with increased risk has been identified. Recurrent attacks of AP have been linked to continued alcohol consumption. Aggressive alcohol intervention has been shown to decrease the risk of recurrences. It is noted that alcoholic AP

progresses to CP in only 15% to 20% cases and does so more frequently in patients with recurrent attacks, among smokers, and with continued alcohol consumption. Patients with alcoholic CP have more symptomatic disease, and their lifespan is significantly shorter compared with the general population. Priority should be placed on educating physicians and the public about the risk of pancreatitis with alcohol consumption and smoking and the benefits of abstinence for primary and secondary prevention. In the absence of targeted therapies for alcoholic pancreatitis, such an approach can be very helpful for improving outcomes in affected individuals and decreasing disease burden among individuals at risk for pancreatitis.

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