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The Epidemiology of Pancreatitis and Pancreatic Cancer

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Abstract

Acute pancreatitis is one of the most frequent gastrointestinal causes for hospital admission in the US. Chronic pancreatitis, although lower in incidence, significantly reduces patients' quality of life. Pancreatic cancer has high mortality and is 1 of the top 5 causes of death from cancer. The burden of pancreatic disorders is expected to increase over time. The risk and etiology of pancreatitis differ with age and sex, and all pancreatic disorders affect Blacks more than any other race. Gallstones are the most common cause of acute pancreatitis, and early cholecystectomy eliminates the risk of future attacks. Alcohol continues to be the single most important risk factor for chronic pancreatitis. Smoking is an independent risk factor for acute and chronic pancreatitis, and its effects could synergize with those of alcohol. Significant risk factors for pancreatic cancer include smoking and non-O blood groups. Alcohol abstinence and smoking cessation can alter progression of pancreatitis and reduce recurrence; smoking cessation is the most effective strategy to reduce the risk of pancreatic cancer.

Keywords

pancreatitis; cancer; epidemiology

Introduction

Acute pancreatitis (AP) caused approximately 275,000 hospitalizations in 2009[1] (an increase of more than 2-fold since 1988[2]) and is the single most frequent gastrointestinal cause of hospital admissions in the US. Although chronic pancreatitis (CP) is lower in incidence and prevalence than AP, CP significantly affects patients' quality of life; it is characterized by chronic abdominal pain, frequent disease exacerbations, and exocrine and/or endocrine insufficiency. Pancreatic cancer has a lower incidence than many other types of cancer, but is the fourth most common cause of death from cancer. We review the epidemiology and risk factors for pancreatitis and pancreatic cancer.

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Descriptive Epidemiology

Incidence, Prevalence, and Trends

The annual incidence of AP[3–5] ranges from 13 to 45/100,000 persons, and CP[5, 6] from 5 to 12/100,000; the prevalence of CP is about 50/100,000 persons[6, 7]. The incidence of pancreatitis and pancreatic cancer in the US are shown in Figure 1[7–9]. Population distributions are mostly reported from the US, Europe, and Japan, but data are emerging from other regions[4]. Variations in disease estimates result from differences in study methodology, difficulties in establishing accurate diagnoses, the use of different diagnostic criteria, and local lifestyle risk factors[10]. Further, analyses that use administrative data or include non-unique patients can increase estimates. There are also regional differences in demographic distributions: alcohol-related pancreatitis is more common in the West and Japan, compared with other Asian countries, and there is wide variation in the prevalence of a form of CP that is endemic to tropical countries (20–125/100,000 persons reported in 2 parts of South India)[11,12].

A large increase in the incidence of AP and a smaller increase in the incidence of CP have been reported in population studies [6, 7, 10]. The increasing incidence of obesity is likely to contribute to that of AP, because obesity promotes gallstone formation—the most common cause of AP. Another major contributor is increased availability and use of tests to measure serum levels of pancreatic enzymes, which detect milder cases of AP but can also result in over diagnosis[13]. In the US, emergency room use of tests to measure serum pancreatic enzymes reportedly increased by more than 60% over a 10-year period[14].

Increases in the prevalence of CP could result from greater availability of high-quality cross-sectional imaging techniques that can detect morphologic changes in the pancreas. Alcohol consumption has been increasing in the developing countries, such as China and India,[15] due to rapid urbanization and increased affluence. This increase would be expected to increase the burden of alcohol-related pancreatitis in these countries. In contrast, alcohol consumption has been generally stable or decreased in many North American and European countries.

The global annual incidence rate for pancreas cancer is about 8/100,000 persons[16]. Adenocarcinoma is the most frequent type of pancreatic cancer; slower-growing endocrine tumors account for only a small fraction of the total burden of disease. As for nearly all cancers, incidence rates of pancreatic cancer vary among countries, with approximate 5- to 7-fold differences between countries with the lowest and highest incidence; rates reported from African countries are low because of insufficient data. There has been a concerted search for environmental factors that might account for this variation. In addition to country-specific differences, subtle geographic and regional differences exist, with countries located on or close to the equator having lower rates than antipodal countries. In 2008, there were an estimated 279,000 new diagnoses of pancreatic cancer worldwide, accounting for 2.2% of all new cases of cancer[17].

Age and Sex

Although equal proportions of men and women develop AP, CP is more common among men. The risk of AP progressively increases with age, whereas CP mainly affects middle-aged individuals. Age and sex distribution differ based on etiology (see Figures 2 and 3). Alcohol-related pancreatitis is more common in men, though sex differences disappear with similar levels of alcohol consumption[18]. Studies are needed to determine whether genetic factors increase risk in men. Pancreatitis in women is more likely related to gallstones, endoscopic retrograde cholangiopancreatography, or autoimmune diseases, or to be

idiopathic. Variations in age and sex distribution among geographic regions likely arise from differences in etiology[19]. Although pancreatitis is uncommon among persons younger than 20 years old, it is increasingly recognized in the pediatric population[20]. Common etiologies of AP in pediatric patients include gallstones, medication, and idiopathic disease[21]. Genetic factors are likely to contribute to unexplained recurrent AP or CP[22, 23].

As for other cancers, fewer than 10% of cases of pancreatic cancer occur among individuals younger than 55 years old, and the median age of onset is 71 years. Figure 4 compares US rates of pancreatic cancer by sex, race, and ethnicity. In all groups, men have higher incidence rates than women.

Race

The risk of pancreatitis is 2–3 fold higher among Blacks than Whites[2,24], and pancreatic cancer rates are considerably higher in Blacks than in any other racial group[9], a disparity similar to that of lung cancer. Little is known about the reasons for the racial disparity—further research is urgently needed. Distributions of lifestyle factors, such as heavy drinking or smoking, are similar among US Blacks and Whites[25]. Studies are needed to determine whether the observed differences result from dietary, genetic, or other factors.

Lifestyle Factors

Alcohol

Although patients who have never consumed alcohol can develop pancreatitis, alcohol appears to increase the sensitivity of the pancreas to injury from other factors (genetic or environmental),[26] and the risk of pancreatitis is undoubtedly increased by alcohol consumption. The prevalence of pancreatitis is increased approximately 4-fold among subjects with a history of alcoholism, compared to those without[27]. The absolute risk of pancreatitis from alcohol consumption is much lower than that for chronic liver disease or cirrhosis, and ranges from 2% to 5% among patients who consume large amounts of alcohol[18,27, 28]. Alcohol use is the single most common cause of CP[29,30] (its attributable risk is about 40%), and after gallstones, is the second-most common cause of AP[10].

Alcohol was shown to increase the risk of pancreatitis in a dose-dependent manner in a recent cohort study[28]. The risk for CP increases at threshold of approximately 5 drinks/day (an odds ratio of 3.1)[31], based on a large case-control study, or at 4 drinks/day, based on a meta-analysis of published literature (a relative risk of 2.5)[32]. These data indicate a clear increase in risk among heavy drinkers, though lower levels of alcohol consumption might not be completely safe—especially among subjects who have had an episode of AP or are diagnosed with CP.

After patients had a first episode of alcohol-related AP, their risk of progression to CP was found to be approximately 14% with complete abstinence or only occasional drinking, 23% with decreased but daily drinking, and 41% with drinking at the same levels as before the AP attack[33]. A randomized controlled trial reported that the risk of recurrence after a first episode of acute alcohol-related AP decreased significantly following repeated counseling against alcohol consumption[34].

Two cohort studies have examined the relationship between pancreatitis and consumption of different types of alcohol[28, 35]. A Danish study associated pancreatitis with consumption of >14 beers/week, but not wine or spirits[28]. A Swedish study associated AP with 5 or more drinks of spirits on a single occasion, but not with beer or wine[35]. One limitation of these analyses was the small numbers of subjects in the heavy-drinking groups, who have the greatest risk of developing pancreatitis. Pancreatitis is observed in all populations,

irrespective of the type of beverage they consume, but the contribution of beverage type to risk requires further study.

With regard to binge drinking, a study compared the number and frequency of hospital admission of patients with AP during the Munich Oktoberfest with 2 other time periods and found no significant increase during this 16-day period of increased beer drinking[36]. In this study, a brief period of increased drinking (above baseline low levels) did not appear to increase the risk of AP, at a population level. The risk seems to be higher in patients with a prior history of heavy drinking, many of whom report an increase in alcohol consumption during the weeks preceding their attack. An interesting study from Netherlands found that about 50% patients with alcohol-related AP developed symptoms 2 days after they stopped drinking,[37] raising questions about whether the amount, duration, and/or withdrawal of binge drinking affects risk for AP.

It is difficult to implicate alcohol as an independent risk factor for pancreatic cancer because of the close association between alcohol and smoking—a proven risk factor for pancreatic cancer. If alcohol affects pathogenesis of pancreatitis, it could promote the effects of other risk factors, such as smoking. Recent studies concluded that heavy drinkers might have an increased risk of pancreatic cancer. Gapstur et al., in a study of non-smokers, observed an increased risk of pancreatic cancer only among persons who consumed more than 3 drinks per day[38]. Examining 10 case-control studies, Lucenteforte et al. found an increased risk of pancreatic cancer among persons who consumed more than 9 drinks per day[39].

Smoking

Since 1982, when smoking was initially reported as a risk factor for CP [40], numerous studies have confirmed this association. Smoking and alcohol are co-factors that increase the risk of pancreatitis. In a multi-center study, ever and current smoking was reported by 71.4% and 47.3% of patients with CP, respectively, at the time of enrollment. Drinking and smoking habits often co-exist, and the prevalence of smoking was found to increase with the amount of alcohol consumed[31].

A meta-analysis of 12 studies of approximately 1500 patients with CP associated levels of smoking with CP. The excess risk for CP was more than 2-fold (a relative risk of 2.4) among subjects who smoked less than 1 pack/day and more than 3-fold (a relative risk of 3.3) among those who smoked 1 or more packs/day. The risk was higher for current smokers (a relative risk of 2.5) and significantly lower among former smokers (a relative risk of 1.4)[41]. Although smoking increases the risk of CP independently of alcohol, the effects of smoking are stronger for alcohol-related CP.

Smoking also increases the risk for AP[42–44]. A Swedish study[43] found that smoking increased the risk for non-gallstone-related (by about 2-fold), but not gallstone-related AP[43]. The risk was especially high in patients who consumed alcohol (defined as ≥400 grams/month), current smokers, and those with ≥20 pack years of smoking. The risk was highest in subjects who had all these characteristics (a relative risk of 4.12); these patients had to stop smoking for 2 decades to reduce their risk level to that of never-smokers.

Smoking has been calculated to attribute 25% of the risk for CP, and continued smoking after a diagnosis accelerates disease progression[45]. Physicians often focus on counseling patients with CP against alcohol consumption and underestimate the role of smoking[46], thereby missing opportunities to counsel patients on smoking cessation or to refer them to behavior modification programs.

The relationship between smoking and pancreatic cancer has been studied extensively; there are nearly 500 references listed in PubMed on this association. Studies have consistently confirmed the relationship between smoking and pancreatic cancer, with smokers having about a 2-fold excess risk compared with non-smokers. This increase in risk is smaller than for lung cancer, but is similar that of other tumors, such as bladder cancer. This could be because the bladder and pancreas each have indirect exposure to tobacco carcinogens.

A recent pooled analysis of 12 case-control studies that included nearly 13,000 patients with pancreatic cancer concluded that current smokers had an odds ratio of 2.2, compared with never smokers[47]. As expected, risk increased in proportion to smoking. For ex-smokers, the odds ratio was 1.2. With smoking cessation, risk gradually decreases, but 10–20 years are required before the smoking-related risk disappears.

The association between exposure to environmental tobacco smoke and the subsequent risk of pancreatic cancer is controversial. Two studies of the same European cohort reported an excess risk of pancreatic but no other cancers after childhood exposure to tobacco smoke. Surprisingly, the risks were as high or higher than expected from direct smoking, so the findings could result from chance or an undetected bias[48, 49].

If smoking doubles the risk of pancreatic cancer, and if approximately 30% of the population smokes, then about 25% of all cases of pancreatic cancer can be attributed to smoking. This makes smoking cessation the single most effective strategy to reduce the burden of pancreatic cancer.

Why is smoking such a strong risk factor for pancreatic cancer? Tobacco smoking releases many carcinogens. Several gene products mediate the degradation of tobacco carcinogens; a recent study examined several detoxifying genes in 455 patients with pancreatic cancer[50]. Variants in genes such as *CYP1B1-4390-GG* and *uridine 5′-diphosphoglucuronosyltransferase* reduced the risk of pancreatic cancer, whereas variants in others, such as *GSTM1*, increased risk. Little is known about the mechanisms by which these genes affect cancer risk, but their products could affect the inflammatory response, fibrosis, cell proliferation, and other processes involved in carcinogenesis [51].

Diet

Over the course of an entire lifetime, each individual consumes several thousand pounds of food; given such exposure, it seems reasonable that diet would affect risk for different digestive diseases and cancer, including those of the pancreas. However, it has been a challenge to establish a link between diet and cancer, and case-control studies (the most common type of epidemiologic studies) are prone to recall bias. Cohort studies in which dietary information is collected before subjects develop cancer are more reliable, but have not provided consistent evidence for an association.

A Mediterranean dietary pattern, when combined with other factors indicative of a healthy lifestyle, protects against pancreatic cancer[52]. Red meats, particularly when cooked at high temperatures, increase the risk of pancreatic cancer[53]. Based on data from more than 500,000 persons in 10 countries, consumption of fruit and vegetables does not decrease the risk for pancreatic cancer[54]. Similarly, carbohydrate intake was not associated with pancreatic cancer risk[55]. The role of dietary factors in the etiology of pancreatitis is unclear. This is an important area for future research—especially with growing evidence for the roles of the intestinal microbiota in health and disease[56].

Obesity

In a population-based study, abdominal adiposity, but not total adiposity or body mass index (BMI), increased the risk for AP, after controlling for demographic and lifestyle factors[57]. The effect was similar for gallstone- and non-gallstone–related AP and for mild and severe AP. Individuals with a waist circumference of >105 cm had a 2-fold increase in risk of AP (a relative risk of 2.37), compared with those with a waist circumference of 75–85 cm. Obesity also increases the severity of AP. In a recent meta-analysis, compared with subjects who had a normal BMI, obese subjects (BMI >30 kg/m^2) had a higher risk of AP (summary relative risk of 1.34) and of severe AP, greater numbers of systemic and local complications, and increased mortality[58]. Central fat distribution has been associated with a systemic inflammatory response in patients with AP[59]. The excess risk from obesity is related to the volume of visceral adipose tissue and the mechanism of injury is related to the pro-inflammatory effects of unsaturated fatty acids generated by lipolysis[60].

Obesity is also a risk factor for several types of cancer, including pancreatic. A meta-analysis of 6391 patients with pancreatic cancer found a relative risk of 1.19 for cancer among obese persons, compared with persons of normal weight[61]. Similarly, a pooled analysis of 14 cohort studies found an increased risk for obese persons, persons who gained weight, and persons with a high waist-to-hip ratio[62]. The available data for obesity are stronger than that for diet, and reinforce the concept that maintaining a healthy body weight can prevent pancreatic cancer.

Diabetes, Drug Exposure, and Blood Type

Diabetes

In 3 large retrospective cohorts, type 2 diabetes mellitus increased the risk for AP by 1.5–3 fold, after controlling for demographic and other risk factors[63–65]. Compared with non-diabetics, the risk was particularly high in younger diabetic patients (incidence rate ratio of 5.26 for individuals younger than 45 years and 2.44 for individuals older than 45 years)[65]. The use of anti-diabetic medications was found to reduce the excess risk[64]. Interestingly, following case reports of an association with AP, a recent study evaluating reports to the US Food and Drug Administration found a greater than 6-fold increase in the risk of AP among users of medications for type-2 diabetes such as sitagliptin (a dipeptidyl peptidase-4 inhibitor) and exenatide (a glucagon-like peptide-1 analogue)[66]. The rate of diabetes is also increasing in many developing countries, likely from rapid urbanization and adoption of Western lifestyles. This increase means that there will be more cases of AP, either related to diabetes itself or other risk factors associated with diabetes (gallstones and hypertriglyceridemia).

There is a bi-directional relationship between diabetes and pancreatic cancer. Clinicians are aware that new-onset diabetes can be a symptom of pancreatic cancer, particularly in low-weight, middle-age, or older patients with no family history of this disease. In a study of subjects with new-onset diabetes, the incidence of pancreatic cancer was about 2.2-fold higher than among non-diabetics. However, the absolute risk is low, because only about 0.5% of newly diagnosed patients with diabetes developed pancreatic cancer during a 6 year follow up[67]. Diabetes develops more frequently among patients with pancreatic cancer than controls for as many as 5 years before a diagnosis of pancreatic cancer[68]. Aggarwal et al. found that 40% of patients with pancreatic cancer had an antecedent diagnosis of diabetes in the preceding 3 years, compared to 3–5% of patients with other forms of cancer[69].

Patients with well-established, longstanding diabetes have an approximate 2-fold increase in risk of pancreatic cancer. The increase appears to apply to patients with adult-onset

diabetes[70,71] and probably those with early-onset or type-I diabetes[72]. Additional studies have found that gestational diabetes increases the risk of pancreatic cancer[73, 74]. Interestingly, drugs used to manage diabetes can either reduce (metformin) or increase (insulin or insulin secretagogues) the risk of pancreatic cancer[75]. In the study that evaluated the risk of AP with sitagliptin or exenatide, diabetics exposed to these agents had an increased risk of pancreatic cancer compared with patients taking other types of anti-diabetic drugs[66]. Randomized, controlled trials are required to confirm this risk. The global increase in the incidence of diabetes could affect the incidence of pancreatic cancer.

Drug Exposure

Medication-induced AP is primarily an idiosyncratic reaction. Many medications have been proposed to cause AP, and this list is likely to increase (for a full review, see Ref [76]). No medications are known to cause CP. Several types of drugs could increase or decrease the risk of pancreatic cancer. A cohort study of more than 133,000 men and women found no protective effect of cholesterol-lowering drugs against pancreatic cancer[77].

Although aspirin and non-steroidal anti-inflammatory drugs (NSAIDS) have been associated with a reduced risk of bowel cancer, 2 meta-analyses of American and European studies published before 2006 did not find that these agents protected against pancreatic cancer[78,79]. More recent studies have yielded somewhat different results. Based on information from the UK General Practice Research Database, Bradley et al. found a reduced risk of pancreatic cancer in patients taking NSAIDS for >5 years (an odds ratio of 0.70)[80]. More recent studies have shown that aspirin use appears to lower the risk of pancreatic cancer[81,82]. These studies were based on data from case–control or cohort studies. Using data from randomized controlled trials of the effects of aspirin use on heart disease, Rothwell et al. noted a substantially reduced risk of pancreatic cancer (a relative risk of 0.25) among subjects exposed to aspirin for >5 years[83]. The association was weaker (a relative risk of 0.84) in a follow-up study of persons who took aspirin in the US Cancer Prevention Study II Nutrition Cohort [84].

Blood Type

For many years, ABO blood group status has been associated with gastric cancer. However, a genome-wide association study and conventional epidemiological studies found that non-O blood type increases the risk of pancreatic cancer. Compared with blood group O, subjects with blood types AO, AA, BO, or BB had odds ratios for pancreatic cancer ranging from 1.3 to 2.4. Although the mechanism of this association is unclear, about 15% 20% of all pancreatic cancers could be associated with non-O blood type[85–87]. In a large US study, no significant association was detected between blood group and CP[88].

Other Risk Factors for Pancreatitis

Gallstones

Gallstones are the most common cause of AP[10]. The prevalence of gallstones in the US adult population is 7%[89]. The risk of gallstone-related pancreatitis increases with age and is higher in women, consistent with the demographic distribution of gallstones. It is important to perform cholecystectomy as soon as feasible after an attack of gallstone-related AP, to eliminate the risk of future attacks. A delay in cholecystectomy increases the risk of recurrence and subsequent attacks could be more severe than the first. Gallstones do not cause CP.

Metabolic Factors

Hypertriglyceridemia is an important but under-recognized cause of acute and recurrent AP. It typically develops in a patient with familial combined hyperlipidemia or familial hypertriglyceridemia who has an additional secondary factor such as uncontrolled diabetes, alcoholism, use of certain medications or during pregnancy. Less frequently, physicians may encounter a patients with familial chylomicronemic syndrome who presents with AP[90]. Although very high serum levels of triglycerides (≥1000 mg/dl) are associated with pancreatitis, a recent population-based study found that after controlling for demographic factors and lifestyle habits, patients with even modest increases in serum levels of triglycerides had an increased risk of AP[91]. On further analysis, the risk was specifically increased in patients with AP from non-alcohol, non-obstructive causes—patients with idiopathic pancreatitis. Although uncommon, hypertriglyceridemia can cause CP[92].

Other uncommon but established metabolic risk factors include hypercalcemia, renal failure, and acidosis. A population-based study reported that subjects with primary hyperparathyroidism had a level of risk of pancreatitis similar to controls[93]. Specific genetic variants were identified in patients with primary hyperparathyroidism who also had pancreatitis[94,95].

Autoimmune Diseases

Celiac disease increases the risk of pancreatitis by about 3-fold (a hazard ratio of 2.85)[96]. The risks of AP and CP are also increased among patients with inflammatory bowel disease, systemic lupus erythematosis, and other disorders, although exact estimates are not available. Fewer than 5% of patients with pancreatitis who undergo evaluation at tertiary centers are diagnosed with autoimmune pancreatitis. Among patients with autoimmune pancreatitis, only 10% 25% have features of AP or CP at the time of presentation[97]. Although autoimmune pancreatitis is considered to be a form of CP, it has distinct clinical and histologic features and responds well to steroid therapy. The incidence and prevalence of autoimmune pancreatitis in Japan in 2007 were reported to be 0.9/100,000 persons/year and 2.2/100,000 persons, respectively[98].

Anatomic Abnormalities and Duct Obstruction

Although some anatomic abnormalities of the pancreas (annular pancreas and ductal stricture) are accepted causes of AP and recurrent AP, the role of other anatomic (pancreas divisum) or functional abnormalities (sphincter of oddi dysfunction) is controversial. In a recent study of patients with recurrent AP or CP, the prevalence of pancreas divisum in patients with variants of the *cystic fibrosis transmembrane receptor* gene (47%) was significantly higher than patients with idiopathic (5%) or alcohol-related (7%) pancreatitis, other related genetic factors (variants in *PRSS1* or *SPINK1*] (16%), or control subjects (7%)[99]. The authors concluded that pancreas divisum by itself does not cause pancreatitis but could act as a cofactor with genetic factors. Prolonged ductal obstruction can cause histologic, structural, and functional changes consistent with CP.

Other Risk Factors for Pancreatic Cancer

Chronic Pancreatitis

A meta-analysis of 6 cohort studies and 1 case-control study found that the pooled relative risk estimate for pancreatic cancer among patients with CP is 13.3[100]. Among individuals with the rare form of pancreatitis found mostly in tropical countries, the association appears to be even stronger[101]. Pancreatic stellate cells link pancreatitis and cancer [102]. One pooled analysis of 5048 patients with pancreatic cancer (in 10 case-control studies) found only a small association between pancreatic cancer and antecedent CP (odds ratio of 2.7)[103],

although this might be because the study included some patients without well-documented CP. Nonetheless, given the low incidence of CP and the low incidence of pancreatic cancer in patients with CP (<5%), CP is a rare cause of pancreatic cancer.

Hereditary Pancreatitis

Hereditary pancreatitis is a rare, inherited form of pancreatitis that phenotypically resembles other forms of pancreatitis except for its early age of onset, strong family history, and significant increase in risk for pancreatic cancer. It is an autosomal dominant disease with about 80% penetrance, and most patients develop symptoms before they are 20 years old. Patients with hereditary pancreatitis have a high risk of developing pancreatic cancer (a pooled relative risk of 69)[100], with a lifetime risk of 40–55%[104–106].

Infectious Diseases

There have been a few studies of associations between viral infections and pancreatic cancer. Hepatitis B, a strong risk factor for liver cancer, has been reported to also lead to pancreatic cancer[107,108]. However, in a population-based study of US veterans, Hepatitis C was not associated with an increased risk of pancreatic cancer[109]. *Helicobacter pylori* infection was found to increase risk for pancreatic cancer by a pooled odds ratio of 1.4, based on a meta-analysis of 6 studies published from 1998 through 2010; there was minimal evidence for heterogeneity among studies[110]. Based on these data, we might expect that the geographic distribution of pancreatic cancer would be similar to that of *H pylori* infection; this is not the case, so further studies of this association are needed.

Disease Progression and Mortality

There are data to indicate that AP progresses to recurrent AP and then to CP, in a disease continuum[33, 111–113]. Overall, about 20% 30% of patients with AP have a recurrence and about 10% develop CP. Progression from AP to CP occurs more frequently with continued exposure to alcohol or smoking and in patients with genetic causes of pancreatitis (hereditary pancreatitis). Patients with pancreatitis should receive appropriate counseling and be referred to rehabilitation services, when appropriate.

AP has an overall low mortality, of approximately 1%[1]. The risk of death increases with age, co-morbidities, and severe disease; in a recent meta-analysis, the risk of death was the highest among patients with both organ failure and infected necrosis[114]. Proportional mortality has decreased over time, likely from better intensive and supportive care, clarity on optimal timing of interventions for complications (surgery, endoscopic, or percutaneous drainage), and increased detection of milder cases. Although data are limited, the population mortality has not decreased[10]. Patients with CP have shorter survival times than the population[7, 115], but most die from non-pancreatic causes, such as other chronic diseases, cancers, or infections. Mortality is high among patients with pancreatic cancer. The number of deaths each year from pancreatic cancer is approximately equal to the number of new cases, and the 5-year survival rate is approximately 6%[9].

Future Directions

Much pancreatic disease research has focused on identifying risk factors, clarifying the relationship between risk factors and disease, and discovering better methods for diagnosis, management, and prevention of pancreatitis. Faster, less-costly methods of genetic analysis, which are rapidly becoming available, will provide much-needed answers to the numerous unsolved questions concerning all types of pancreatic disorders.

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Biographies

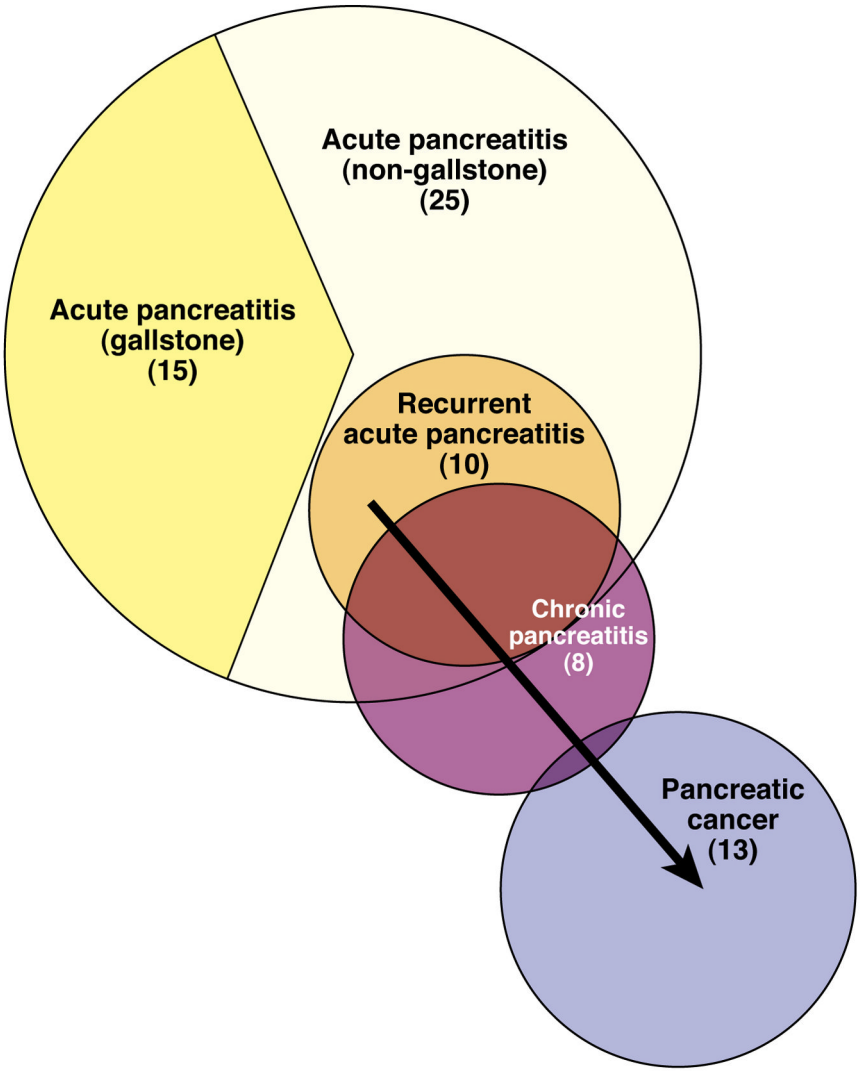

Figure 1. Incidence Rates for Pancreatitis and Pancreatic Cancer in the US

Numbers in parenthesis indicate approximate yearly incident rates per 100,000 persons. Arrow indicates relationship between benign and malignant disease. Recurrent AP develops predominately in patients with non-gallstone related pancreatitis, although it can develop in patients with gallstone-related pancreatitis when cholecystectomy has been delayed or refused.

Ref. 8,9,24

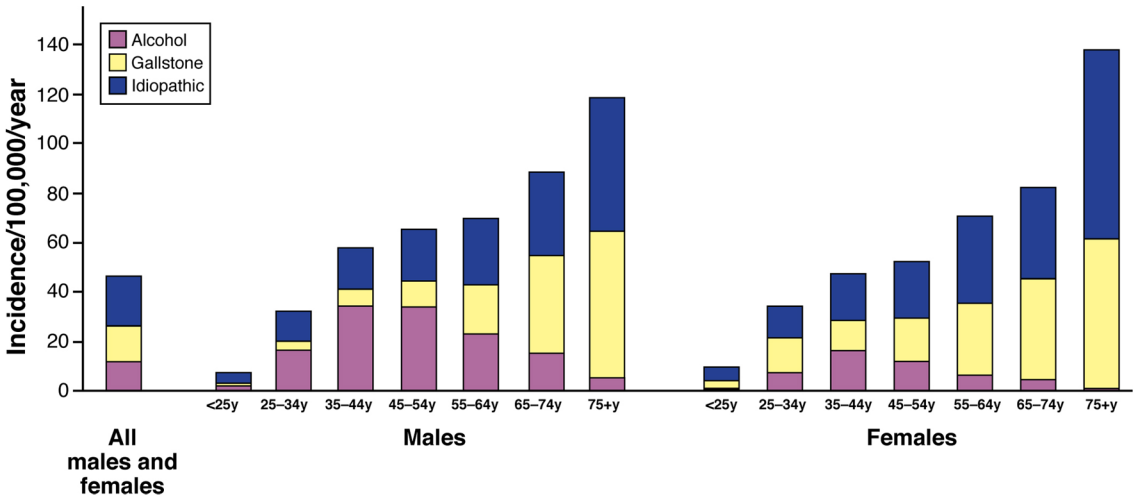

Figure 2. Incidence of AP

Graph shows incidence from 1996–2005 in White and Black residents of Allegheny County, PA, US, based on age-group, sex and etiology.

Source: Allegheny County census data (http://www.cdc.gov/nchs/nvss.htm); pancreatitis data (Ref. 113). Incidence data is shown only for patients with alcohol, gallstone or idiopathic etiology. Rate for all patients is age, sex and race adjusted to 2000 US population.

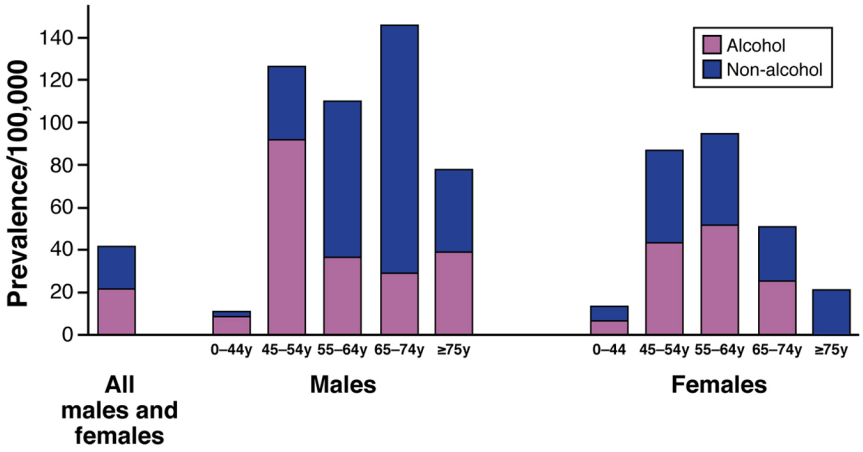

Figure 3. Prevalence of CP

Graph shows prevalence of CP in 2006, in Olmsted County, MN, US, based on age-group, sex and etiology.

Data in part from Ref. 7 (with permission). Rate for all patients is age and sex adjusted to 2000 US White population.

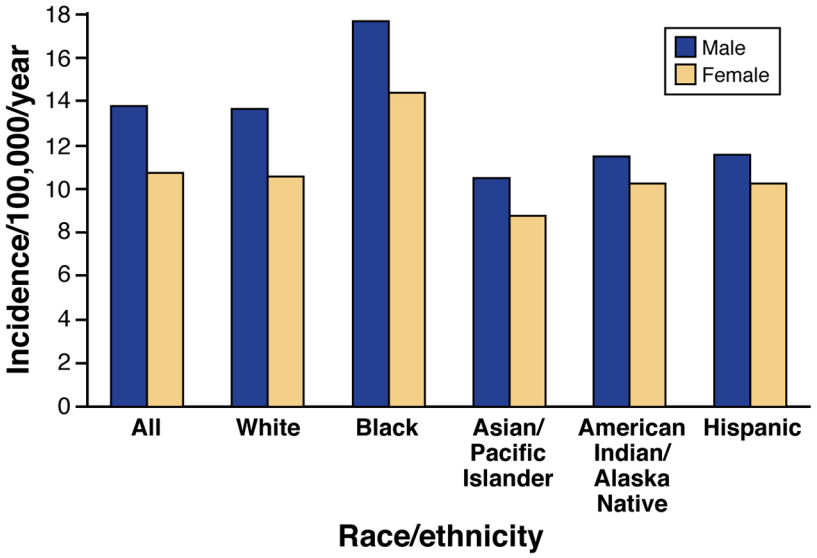

Figure 4. Incidence of Pancreatic Cancer

Incidence of pancreatic cancer from 2005 to 2009 in the US, based on sex and racial groups. Ref. 9