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Brief communication

Risk factors for pancreatitis in older women: the Iowa Women's Health Study



Anna E. Prizment PhD, MPH^{a,c,*}, Eric H. Jensen MD^b, Anne M. Hopper MPH^c, Beth A. Virnig PhD^d, Kristin E. Anderson PhD, MPH^{a,c}

^a Division of Epidemiology & Community Health, School of Public Health, University of Minnesota, Minneapolis

^b Division of Surgical Oncology, University of Minnesota Medical School, Minneapolis

^c Masonic Cancer Center, University of Minnesota, Minneapolis

^d Division of Health Policy and Management, School of Public Health, Masonic Cancer Center, University of Minnesota, Minneapolis

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ABSTRACT

Purpose: Pancreatitis—an inflammation of pancreas—is a severe and costly disease. Although many risk factors for pancreatitis are known, many pancreatitis cases, especially in elderly women, are of unknown etiology.

Methods: Risk factors for acute pancreatitis (AP) and chronic pancreatitis (CP) were assessed in a prospective cohort ($n = 36,436$ women, aged ≥ 65 years). Exposures were self-reported at baseline. Pancreatitis was ascertained by linkage to Medicare claims (1986–2004) categorized by a physician as follows: “AP”, one AP episode ($n = 511$) or “CP”, 2+ AP or 1+ CP episodes ($n = 149$).

Results: Multivariable odds ratios (ORs) and 95% confidence intervals for AP and CP were calculated using multinomial logistic regression. Alcohol use was not associated with AP or CP. Heavy smoking (40+ vs. 0 pack-years) was associated with a twofold increased OR for CP. For body mass index greater than or equal to 30 versus less than 25 kg/m², the ORs were 1.35 (1.07–1.70) for AP (P trend = .009) and 0.59 (0.37–0.94) for CP (P trend = .01). ORs for AP and CP were increased for hormone replacement therapy use, heart disease, and hypertension. There were positive significant associations between protein and total fat intake for CP and AP.

Conclusions: We identified factors associated with AP and CP that may be specific to older women.

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Introduction

Pancreatitis, an inflammatory condition leading to pancreatic tissue damage, causes substantial morbidity and mortality [1,2]. Pancreatitis develops when digestive enzymes produced by the exocrine pancreas become activated in the pancreas instead of the small intestine, causing inflammation and tissue damage in the pancreas [2].

Pancreatitis can be acute pancreatitis (AP), with sudden onset and usually resolving within several days, or chronic pancreatitis (CP), occurring over many years. Annually, approximately 210,000 people with AP are admitted to the hospital in the United States; about 5% of all AP patients die [2,3]. CP occurs when pancreatic inflammation does not completely resolve and is stable or worsens over time, causing permanent tissue damage [2]. Diagnosing

pancreatitis (AP or CP) may be difficult; it requires that two of three criteria (clinical presentation with abdominal pain, elevated amylase or lipase, or radiographic evidence) be met [3]. Symptoms of an exacerbation of CP are often the same as AP [4].

Established causes of pancreatitis include gallstones, heavy alcohol use, and hereditary disorders; potential risk factors include use of certain medications, smoking, diet rich in fat and proteins, metabolic factors (e.g., hypertriglyceridemia, hypercalcemia) [1,2,4–6]. Yet, approximately 20% of AP and CP cases are considered idiopathic with no obvious risk factors [7–9]. Because there is no specific treatment for pancreatitis, understanding the etiology of this disease is critical for developing preventive and therapeutic approaches. In this study, we characterized risk factors for AP and CP among 36,436 women aged 65 years and older in the prospective cohort—Iowa Women's Health Study (IWHS).

Materials and methods

The IWHS has been described in detail [10,11]. Briefly, 41,836 postmenopausal women aged 55 to 69 years were recruited at

* Corresponding author. Division of Epidemiology & Community Health, School of Public Health, University of Minnesota, 1300 S. 2nd Street Suite 300, Minneapolis, MN 55454. Tel.: +1 612-626-0250.

E-mail address: prizm001@umn.edu (A.E. Prizment).

baseline (1986). Subjects completed a baseline and five follow-up questionnaires addressing demographics, anthropometrics, lifestyle, medical history, hormone replacement therapy (HRT), diet, physical activity, and other factors [10]. Annual linkage to the Iowa Surveillance, Epidemiology, and End Results registry provided cancer incidence, whereas linkage to the National Death Index provided mortality [10]. The University of Minnesota Institutional Review Board approved this study, and all participants gave consent.

The data for IWHS participants older than 65 years were linked to Centers for Medicare Services claims (1986–2004) by social security number, first and last name, and date of birth [11], as U.S. residents become eligible for Medicare at 65 years. Linkage to participants older than 65 years was successful for 99% of the cohort members alive at 65 years [12]. Pancreatitis cases were ascertained through Medicare hospital, carrier, and outpatient claims [13]. Women with one or more hospitalizations or greater than or equal to two claims from the outpatient or carrier files with an *International Classification of Diseases, Ninth Revision* diagnosis code 577.0 (AP) or 577.1 (CP) were selected and reviewed by a physician. The physician categorized patients as definite, probable, or uncertain pancreatitis. We were conservative and excluded “uncertain” cases, that is, cases with insufficient data to confirm pancreatitis. Pancreatitis cases were categorized as AP, if women had one AP episode and CP, if women had two or more episodes of AP that were at least 6 weeks apart or one episode of CP. Also, women were excluded if their first pancreatitis episode was within ± 6 months of Surveillance, Epidemiology, and End Results–identified gastrointestinal cancer.

We used multinomial logistic regression to calculate odds ratios (ORs) with 95% confidence intervals (CIs) for AP and CP in relation to body mass index (BMI), smoking (status and pack-years), heart disease or attack, diabetes, hypertension, HRT use, alcohol use, dietary factors (all assessed at 1986 baseline), and aspirin use (assessed at 1992).

All models were adjusted for age at the time of Medicare enrollment. The models for BMI and smoking were adjusted for each other. All other models were adjusted for age, Medicare enrollment, BMI, and smoking status and pack-years. Additionally, analyses of dietary factors were adjusted for total energy intake. ORs and *P* values for trend were computed using SAS software, Version [9.3] of the SAS System for Windows. Tests for trend were conducted by including a categorical variable as an ordinal continuous variable in the model.

Results

During follow-up through 2004, 511 AP and 149 CP eligible cases were identified among 36,436 women older than 65 years (mean age \pm SD at enrollment was 65.8 ± 1.6 years; 99.2% white). The mean ages of the AP and CP diagnosis were 75.3 ± 5.5 and 73.3 ± 5.5 years, respectively. At baseline, 23% of the cohort were obese, 14% were current smokers, and 43% consumed alcohol (Table 1).

Cigarette smoking was associated with CP for more than 40 versus 0 pack-years with an OR = 2.03 (95% CI: 1.23–3.34; *P* trend = .02). BMI was positively associated with AP and inversely associated with CP; for BMI greater than or equal to 30 versus less than 25 kg/m², the ORs were 1.35 (95% CI: 1.07–1.70; *P* trend = .009) and 0.59 (95% CI: 0.37–0.94; *P* trend = .01), respectively (Table 2). ORs for AP and CP were increased for HRT use (18% for AP and 97% for CP), heart disease (43% for AP and 94% for CP), and hypertension (37% for AP and 47% for CP). We found an association between aspirin use ≥ 6 times/wk and AP, OR = 1.44 (95% CI: 1.08–1.91) versus no aspirin use (*P* trend = .04). We did not observe

Table 1

Selected characteristics of the IWHS participants

Characteristics ^{a,†}	N	%
Age at enrollment (y)		
65–66	26,763	73.5
67–70	9165	25.2
>70	508	1.4
Education		
Less than high school	7053	19.4
High school graduate	15,183	1.2
Greater than high school	14,101	38.8
BMI mean, kg/m ² (SD)		
Normal weight (<25.0)	14,441	39.6
Overweight (25.0–29.9)	13,483	37.0
Obese (≥ 30.0)	8512	23.4
Physical activity		
Inactive	16,826	47.1
Moderately active	9875	27.7
Very active	8994	25.2
Smoking status		
Never	23,766	66.3
Former	6909	19.3
Current	5185	14.5
Pack-years of smoking		
None	23,766	66.8
1–19	4823	13.6
20–39	3959	11.1
≥ 40	3008	8.5
Alcohol consumption		
No	20,566	56.4
Yes	15,870	43.6
Heart disease/attack		
No	31,669	90.3
Yes	3412	9.7
Diabetes		
No	34,179	93.8
Yes	2242	6.2
Hypertension		
No	22,291	62.6
Yes	13,327	37.4
HRT use		
No	22,300	61.5
Yes	13,971	38.5
Aspirin use (times/wk) [†]		
None	8218	28.3
\leq Once	9593	33.0
2–5	5125	17.6
≥ 6	6111	21.0

^a Frequencies may not add up to the total because of missing values.

[†] All characteristics (except age at enrollment and aspirin use assessed in 1992) were assessed at baseline (1986).

associations of alcohol or self-reported diabetes with either AP or CP (Table 2).

In the analysis of dietary factors and AP, we found an increased risk associated with total and saturated fat intake. For CP, we observed marginally statistically significant trends for saturated fat and protein intakes.

Discussion

In our study of women older than 65 years, we confirmed several known risk factors for pancreatitis. Consistent with previous studies [1,14], heavy cigarette smoking (40+ vs. 0 pack-years) was associated with a twofold increased risk for CP, whereas BMI was associated with a moderately increased risk for AP, as shown in two meta-analyses [15,16]. The potential mechanisms for a BMI–AP association may be through inflammation accompanying obesity and/or gallstone disease, which is a known risk factor for pancreatitis [1]. As gallstone disease is common in obese people, it may mediate the obesity–AP association [17]. Furthermore, in our study, BMI was inversely associated with CP, which is most likely

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